Summary of the Safety and Effectiveness of Mentor's Round Low Bleed Silicone Gel-Filled Implants in Patients who are Undergoing Primary Breast Augmentation, Reconstruction, or Revision

3-Year Core Gel Clinical Study Update
August 2004

27 Aug 2004

TABLE OF CONTENTS

LIST OF APPENDICES

Appendix	Title
A	Deviations
B	List of Investigators and IRBs
C	Financial Disclosure
D	Tables

LIST OF APPENDIX D TABLES

Table	Title
20.1	Functional Living Index: Cancer (FLIC)
20.2	Functional Living Index: Cancer (FLIC) by Device Placement
21	Global Patient Satisfaction
22.1	Incidence of Postoperative Complications and Reoperations by Time Period (Patient Level)
22.2	Incidence of Postoperative Complications and Reoperations by Time Period (Implant Level)
23.1	Prevalence of Postoperative Complications and Reoperations by Time Period (Patient Level)
23.2	Prevalence of Postoperative Complications and Reoperations by Time Period (Implant Level)

1.0 INTRODUCTION

Mentor is conducting a 10-year prospective clinical study designed to collect safety and effectiveness data associated with the implantation of smooth and textured Mentor Silicone Gel-Filled Breast Implants. The study was designed and conducted in accordance with the Food and Drug Administration's then current then current "Guidance for Saline, Silicone Gel, and Alternative Breast Implants: Final Guidance for Industry and FDA," and in consultation with experts from a variety of medical disciplines.

Clinical indications for Mentor Silicone Gel-Filled Breast Implants include aesthetic augmentation of the female breast for cosmetic purposes, reconstruction of the female breast following mastectomy or other conditions that result in deformities of the breast, and revision of pre-existing implants.

Mentor is submitting this update to the PMA submitted in December 2003 with patient follow-up data through 3 years post-implantation. Patients will continue to be followed by their physicians at 4, 5, 6, 7, 8, 9, and 10 years post surgery.

2.0 STUDY OBJECTIVES

The objective of this clinical study is to assess the safety and effectiveness of smooth and Siltex™ (textured) surface Mentor Silicone Gel-Filled Breast Implants in women who are undergoing primary breast augmentation, primary breast reconstruction, or revision.

2.1 Safety

Safety is based on the incidence, severity, method of resolution, and duration for all complications and is calculated on a per patient and per implant basis.

2.2 Effectiveness

The primary effectiveness assessments are changes in chest circumference and bra cup size following the implantation procedure.

Secondary effectiveness objectives of the study are self-reported changes in Quality of Life questionnaire results.

3.0 STUDY DESIGN

This is a prospective, open-label, multi-center clinical trial involving the Mentor Silicone Gel-Filled Breast Implant, specifically the smooth surface device and Siltex™ textured surface device, to include augmentation, reconstruction, and revision mammoplasty patients in a 10-year clinical study setting.

The Augmentation cohort included patients who have post-lactational mammary involution or wish general breast enlargement.

The Reconstruction cohort included patients with loss of breast due to mastectomy or with deformities secondary to disease, malignancy, trauma, or congenital deformity.

The Revision cohort included patients with previous breast augmentation or reconstruction with silicone or saline filled implants.

Once a patient was enrolled in a particular cohort, she was not moved to another cohort if she had additional breast surgery. For example, an augmentation patient did not become a Revision patient if she had her original study devices removed and was reimplanted with study devices. She remained an augmentation patient regardless of subsequent surgery.

A subset of these three cohorts was included in an MRI (Magnetic Resonance Imaging) substudy to evaluate silent rupture of the Mentor Silicone Gel-Filled Breast Implant.

Patient enrollment for this study began on September 12, 2000 and was completed November 28, 2001, and a 10-year follow-up is planned for each patient. Patients will continue to make active follow-up visits at 4, 5, 6, 7, 8, 9, and 10 years post-surgery.

3.1 Study Population

One-thousand-seven (1,007) female patients (551 Augmentation, 251 Reconstruction, and 205 Revision patients) were enrolled by 40 Investigators. Patients were considered enrolled in the study upon implantation. Some sites were designated to recruit only the primary Augmentation cohort, others were designated to recruit only the primary Reconstruction cohort, while others could recruit both Augmentation and Reconstruction cohorts. All sites were able to recruit the Revision cohort.

Patients meeting the following inclusion criteria were eligible to participate in the trial:

- Patient was genetic female and at least 18 years old
- A candidate for:
  - Primary breast augmentation (for post-lactational mammary involution or general breast enlargement)
  - Primary breast reconstruction (for cancer, trauma, surgical loss of breast or congenital deformity)
  - Revision surgery (previous augmentation or reconstruction with saline-filled or silicone gel-filled implants)
- Signs the Informed Consent
- Agrees to follow the procedures for explant analysis
- Agrees to comply with follow-up procedures, including returning for all follow-up visits

Patients with any of the following conditions were excluded from the trial:

- Patient is pregnant
- Has nursed a child within three months of study enrollment.
- Been implanted with any silicone implant other than breast implants
- Confirmed diagnosis of rheumatic disease
- Currently has a condition that could compromise or complicate wound healing (except Reconstruction patients)
- Patient in Augmentation cohort and has diagnosis of active cancer of any type
- Infection or abscess anywhere in the body
- Demonstrates tissue characteristics which are clinically incompatible with implant (e.g. tissue damage resulting from radiation, inadequate tissue, or compromised vascularity)

- Possesses any condition, or is under treatment for any condition which, in the opinion of the investigator and/or consulting physicians(s), may constitute an unwarranted surgical risk
- Anatomic or physiologic abnormality which could lead to significant postoperative adverse events
- Demonstrates characteristics that are unrealistic/unreasonable with the risks involved with the surgical procedure
- Premalignant breast disease without a subcutaneous mastectomy
- Untreated or inappropriately treated breast malignancy, without mastectomy
- Implanted metal or metal devices, history of claustrophobia or other condition that would make a MRI scan prohibitive

Pursuant to FDA guidance, a subset of patients was randomly selected to undergo MRI scans.

3.2 Study Procedures

Participating patients were evaluated preoperatively and postoperatively. All data collected during the study were recorded on the appropriate Case Report Forms (CRFs). Clinical management of the patient was carried out according to the usual procedures employed by the Investigator consistent with the study protocol. Study procedures are outlined below in Table 3.2-A.

At the baseline visit. if the rheumatology physical examination revealed evidence of possible connective tissue disorders, the patient was referred to a rheumatologist for evaluation before being enrolled in the study. If the rheumatologist diagnosed a rheumatic disease the patient was excluded from the study. The Investigator also recorded the patient's circumferential chest size, bra cup size, and baseline nipple and breast sensitivity. At the time of the surgical procedure the appropriate CRFs were completed by the Investigator.

Table 3.2-A: Study Evaluation Schedule Summary

Data Collected	Baseline	Operative	Postoperative		
			6 Months	12 & 24 Months	3 - 10 Years[1]
Inclusion/Exclusion Criteria	X				
Patient Informed Consent	X				
Demographics/Physical Exam	X				
Medical/Breast History	X				
Breast Measurements	X		X	X	X
Mammogram Report (if available)	X		X	X	X
Quality of Life[2]	X			X	X
Nipple/Breast Sensitivity Assessment	X		X	X	X
Capsular Contracture			X	X	X
Rheumatology Assessment	X			X	X
Operative Information		X			
MRI Scan[3]				X	X[3]
Adverse Events			X	X	X
			And Upon Occurrence		
Reoperations and Reimplantations			Upon Occurrence		

1 Annually at 3, 4, 5, 6, 7, 8, 9, and 10 years.
2 Rosenberg Self Esteem Scale, SF-36, Body Esteem Scale, Tennessee Self-Concept Scale, FLIC (Cancer patients only)
3 MRI scan performed on a subset of patients at 1, 2, 4, 6, 8, and 10 years

Participating patients will be followed for 10 years following prosthesis implantation. Data were collected at 6 months and at 1, 2, and 3 years following implantation. Data will continue to be collected at 4, 5, 6, 7, 8, 9, and 10 years following implantation. Postoperatively, breast examinations were conducted and information about complications was collected from the patients at each follow-up visit. The patient's circumferential chest size and bra cup size, nipple and breast sensitivity, capsular contracture assessment, concomitant medications and surgeries were recorded. The Rheumatic Disease Diagnosis Questionnaire and the Quality of Life questionnaires were collected postoperatively beginning at the 1-year follow-up visit. MRI scans were performed on a subset of patients at the 1 and 2-year visits, and will continue to be completed at the 4, 6, 8, and 10-year visits. Mammography was not a study requirement, however, if the patient underwent a mammogram, results were reported on the postoperative CRF.

The Rheumatic Disease Diagnosis Questionnaire captured rheumatic disease, rheumatic symptom, and rheumatic physical exam data. If the rheumatological exam revealed evidence of a possible rheumatic disease, the patient was referred to a rheumatologist. If the rheumatologist diagnosed a rheumatic disease, the confirmed diagnosis was reported on the Adverse Event CRF.

Quality of Life instruments for the study included the Rosenberg Self-Esteem Scale, the Body Esteem Scale, the Tennessee Self-concept Scale (TSCS), the SF-36 Health Survey Scale, and the Manitoba Cancer Treatment and Research Foundation Functional Living Index Scale: Cancer (FLIC) (cancer patients only).

3.3 Study Windows

The patient was considered in compliance with the visit schedule if she was evaluated within the following visit windows relative to the date of surgery:

- 6 Months: ± 4 weeks
- 1 Year: ± 6 weeks
- 2 Years: ± 8 weeks
- 3, 4, 5, 6, 7, 8, 9 and 10 years: ± 4 months

If a patient missed two consecutive follow-up visits, she was withdrawn from the study and considered lost to follow-up.

3.4 Interim Visits

Interim visits may have occurred if any complication or other problem arose. The Investigator was instructed to report complications when they occurred.

3.5 Secondary Procedures/Reimplantation

For each instance of explantation, revision, re-implantation or other secondary procedures, the Secondary Procedures Report CRF was completed. If a new study device was implanted, the Reimplantation Report was completed.

3.6 Device Descriptions

The Mentor Silicone Gel-Filled Breast Implants that are the subject of this PMA consist of a silicone elastomer shell assembly filled with silicone gel. They are available in smooth and textured surfaces in a round design in varying sizes with three different profiles. The products are single lumen devices. The devices use the same materials and design for the shell (i.e., the same dimethyl/diphenyl silicone copolymer layer sandwiched between inner and outer layer(s) of dimethyl silicone) and gel-filler. This shell design minimizes silicone bleed through the shell as discussed in the Mechanical Module of this PMA. The only difference between the smooth and textured devices is that the textured layer is composed of a separate silicone elastomer sheet that is vulcanized to the shell and a textured patch is used in lieu of a smooth patch. The different device shapes are achieved by using differently shaped mandrels to dip the shells.

All gel-filled mammary prostheses are sold packaged in double-sealed nested thermoforms, each with a Tyvek lid, and dry-heat sterilized. Devices are shipped to customers in individual boxes.

3.7 Data Quality Assurance

Individual patient case report forms were reviewed and verified against source documents by Mentor, or their designee, in the course of monitoring the clinical investigation. Field monitoring visits were conducted at all sites, and were performed by trained clinical monitors. The review included examination of Investigator documents, case report forms, and query resolutions.

Subsequent processing and analysis of the data was performed by Abt Associates Clinical Trials (AACT). The information on the case report forms was entered and verified using the Clintrial™ System version 3.3.3 (Domain Pharma Corporation, 10 Maguire Road, Suite 110, Lexington, MA 02421). Data were then checked using a computerized edit system. Values that were outside of specified ranges, invalid, or inconsistent with other data were queried. A randomly selected group, representing 10% of patients had 100% of their data audited for accuracy. Selected database tables were 100% audited for accuracy.

4.0 STATISTICAL METHODS

This PMA update is being submitted based upon data for patients with 3-year postoperative data, seen on or prior to 25 June 2004. All analyses included data up to and including three years of follow-up since the original implant surgery date. The date of database lock was 15 July 2004.

If a study breast implant was explanted, data up to and including the visit of the explantation were included in all safety and effectiveness analyses. Any data captured on the case report form for the explanted breast that were recorded after the explantation occurred were not analyzed. Data for a contralateral study implant that was not removed were still included in all safety and effectiveness analyses. Likewise, the patient was still included in "by patient" analyses.

If both breast implants were explanted and not reimplanted with study devices, that patient was discontinued, and any safety data for the patient collected after the second explantation were not analyzed. An exception to the above is the analysis of postoperative complications and reoperations after explantation with replacement by a study device. In this case, these patients remained in the study, and the results were reported in the study data tables.

Continuous variables were summarized using descriptive statistics (mean, median, standard deviation, minimum, and maximum). Categorical data were summarized using frequency counts.

4.1 Patient Group Definitions

The cohorts were stratified according to the protocol-specified patient and device grouping classifications:

- *Bilateral procedure patients having one breast undergoing reconstruction and the other augmentation were* classified as Reconstruction patients. The device classifications were one reconstruction and one augmentation.
- *Bilateral procedure patients having one breast undergoing revision and the other augmentation* were classified as Revision patients; the device classifications were one revision and one augmentation.
- *Bilateral procedure patients having one breast undergoing revision and the other reconstruction* were classified as Revision patients; the device classification was one revision and one reconstruction.
- *Mixed Revision patients* included all patients having a bilateral revision procedure where one breast had a previous reconstruction procedure and the other breast had a previous augmentation procedure.

- *Mixed post-mastectomy patients* included all patients having an immediate reconstruction procedure on one breast and a delayed reconstruction procedure on the other breast.
- *Delayed post-mastectomy patients* included unilateral patients having delayed post-mastectomy reconstruction in addition to all bilateral patients having a delayed reconstruction procedure on one breast and a reconstruction procedure other than immediate post-mastectomy reconstruction on the other breast.

4.2 Protocol Deviations

There were two protocol deviations that were not reported in the Clinical Module of the PMA submitted in December 2003. Two of the Core patients had an informed consent with a subject signature date after the surgery date. The patients were: 407-031-LKG and 423-022-SWC.

In both cases, the Investigator stated that the consent was read prior to the implant surgery. In one instance, the Investigator said the patient actually signed the consent prior to surgery, but had dated it with the wrong date.

These deviations did not affect patient safety, as both patients read the protocol prior to surgery. In addition to being reported to Mentor, this deviation was reported to the relevant IRBs. The two patients remained in the study, continued to be followed, and their data were reported in the analysis.

4.3 Demographic and Baseline Characteristics

Demographic variables (such as age, weight, and height) and other baseline characteristics (physical examination, medical/breast history, and rheumatology assessments) were summarized using either descriptive statistics; specifically the mean, median, standard deviation, and range for continuous variables, or frequency counts for categorical variables. In calculating percentages, the denominator is the number of patients without missing data.

4.4 Operative Characteristics

Operative characteristics (e.g., surgical approach, surgical placement, incision size, and implant type) were tabulated using frequency counts. In calculating percentages among patients, the denominator is the number of patients without missing data. With regard to breasts, the denominator is the number of implanted breasts without missing data.

4.5 Safety Analysis

This safety analysis was conducted in accordance with the FDA 13 January 2004 ""Draft Guidance for Industry and FDA Staff – Saline, Silicone Gel, and Alternative Breast Implants," as well as conversation with FDA subsequent to the December 2003 PMA submission.

All study patients undergoing implantation with a Mentor study device were included in the safety analyses. Safety analyses were based upon events having an onset date calculated to be within 0-6 months, >6-12 months, or >12-24 months of the initial implant surgery, in addition to overall events for the 0-24 month time period. The analysis also included complications and reoperations after explantation with replacement by a study device.

The safety analysis performed included:

- Analysis of complications by Kaplan-Meier Cumulative Incidence Rate
- Treatment and resolution of complications
- Reoperations and explants
- Complications after reimplantation
- Prevalence and incidence of complications
- Cox regression
- Deaths
- Reproduction and lactation complications
- Breast cancer complications
- Connective tissue/autoimmune/rheumatology disease complications
- Mammography
- Rupture, Possible Rupture, Extracapsular Silicone Gel, and the MRI Substudy

4.5.1 Postoperative Complications and Reoperations

For analysis in this report, data concerning complications and reoperations through three years follow up (calculated from the date of implant surgery to date of event onset) are presented. It is important to note that all surgical procedures have a small risk of complication inherent to the surgery itself. These possible complications include infection, hematoma, seroma, scarring, and nerve damage, and those related to anesthesia.

Complications are presented by individual event, and by cosmetic or non-cosmetic events defined as follows:

- *Cosmetic:* asymmetry, hypertrophic scarring of the skin, ptosis, patient requested size change, and wrinkling
- *Non-cosmetic:* capsular contracture, breast pain not associated with any other complication, breast and nipple sensation changes, calcification, delayed wound healing, extrusion, granuloma, hematoma, infection, lymphadenopathy, necrosis, new diagnosis of breast cancer or rheumatic disease, position change, rupture, seroma, and lactation difficulties. When discussed in the remainder of this submission, "capsular contracture" refers to capsular contracture, Baker Grade III and IV.

Reoperations are stratified and presented by:

- Any reoperation
- Explantation with replacement
- Explantation without replacement

Procedures performed for staged reconstruction (nipple tattooing and nipple reconstruction) were excluded from all reoperation analyses. These procedures are an inherent part of the reconstruction process. Reconstruction patients, who required tissue expansion, were enrolled in the study subsequent to expander removal.

Patient analyses are presented separately for Augmentation, Reconstruction, Revision, and patients overall. All levels of severity are included in the analyses, except for mild occurrences of the following: asymmetry, breast pain, calcification, implant malposition/displacement, nipple sensation changes, breast sensation changes, nipple complications, and wrinkling. All implant level analyses are presented by reason for implantation (Augmentation, Reconstruction, Revision, and Overall).

4.5.1.1 Incidence of Postoperative Complications and Reoperations

Complication and reoperation incidence rates were calculated at both the patient and implant level. Breast side was not specified for systemic complications; these complications were reported at the patient level only. If the same event (complication or reoperation) occurred in a patient and it was determined to be a new event (different onset dates), that patient was counted as having two events of the same type.

The total number and percentage of patients, implants, and events experiencing cosmetic complications, non-cosmetic complications, reoperations, and any complication or reoperation are presented by indication (Augmentation, Reconstruction, Revision, and Overall).

The total number of any complications, cosmetic, non-cosmetic, and specific complications categorized by severity, resolution, and treatment required was tabulated by complication. Duration of each event was also summarized.

For tabulation of events, if the same event occurred more than once in the same patient or implant, the event was counted more than once.

4.5.1.2 Cumulative Incidence of Postoperative Complications and Reoperations

The cumulative incidence of complications and reoperations (i.e., the proportion of patients or implants with a given complication) was estimated using Kaplan-Meier analysis using the time of occurrence calculated as the number of days from the date of the implant procedure to the onset date of the event (complication or reoperation). For these Kaplan-Meier analyses of cumulative incidence, the patient was counted only once regardless of whether the patient had bilateral or unilateral implants. Additionally, if a patient experienced more than one event of the same type over the course of the study, only the first event was included in the analyses.

The following Kaplan-Meier estimates are presented at monthly intervals:

- Proportion of patients and implants experiencing infection
- Proportion of patients and implants experiencing capsular contracture assessment of Baker Class III and IV combined
- Proportion of patients and implants experiencing rupture
- Proportion of patients and implants experiencing any reoperation
- Proportion of patients and implants experiencing explantation regardless of replacement
- Proportion of patients and implants experiencing any complication or reoperation.

Complications and reoperations associated with a given breast occurring after explantation of an implant from that breast were excluded from these analyses (they are reported on in separate tables). Analyses are presented separately for patients and implants. Any complications and reoperations occurring after explantation of the initial study device with replacement using a new study device were analyzed separately in a similar manner to that above. The Kaplan-Meier estimates were based on time from implant replacement to onset date of the complication or reoperation.

4.5.1.3 Reoperation Characteristics

Information regarding reoperation (type of reoperation, device type, primary reason for reoperation, and primary reason for reoperation after explantation) within three years calculated from the date of the initial implant procedure to the date of the reoperation was tabulated at both the patient and implant level. Percentages among patients were based upon the number of patients within each indication (Augmentation, Reconstruction, Revision, and overall) having a reoperation since the initial surgical procedure. Percentages among implants were based upon the number of implants (implanted for Augmentation, Reconstruction, Revision, and overall) for which a reoperation was performed since the initial surgical procedure. As the Investigator selected one primary reason for each reoperation, a hierarchy of reoperation reasons was not used.

4.5.1.4 Open Ended Comments

When the grammatical structure of an "other" open-ended comments fields was confusing or incomplete, the entire study form and/or patient file was reviewed and assessed in order to adequately determine into which category the open ended comment was recoded. In some cases, the Investigator's office was contacted to clarify the response.

4.5.1.5 Cox Regression Analyses

Cox regression analyses were conducted to examine whether specific patient, device, and surgical characteristics are risk factors associated with clinical outcomes.

The Cox proportional hazards model was chosen because of its appropriateness as a method to analyze the occurrence and timing of events with censoring and covariates. These models were implemented using the patient rather than the implant as the unit of analysis. Therefore the outcome variables, as well as the explanatory variables, were defined on the patient level. If a complication was reported for either breast, then the outcome for the patient was a "yes" in the regression. The overall significance of each variable was tested at a significance level of 0.05 using the Wald chi-square test statistic. Each model was analyzed separately for Augmentation, Reconstruction, and Revision patients.

Outcome variable (Complications) included:

- Infection
- Implant rupture
- Capsular contracture
- Nipple sensitivity (unacceptably high or low separately)
- Breast sensitivity (unacceptably high or low separately
- Explantation for any reason (with replacement and without replacement)
- Any reoperation

In the model, explanatory variables were defined as follows:

- Age (in years) was calculated as the difference between date of surgery and date of birth and was included in the models as a continuous variable.
- Race was classified as Caucasian or "Other Race." Caucasian race was used as the reference category. Patients missing race classification were included in the "Other Race" category.
- Smoking status was classified as yes or no. Nonsmokers were used as the reference category.
- Surgical approach was classified as periareolar, inframammary, transaxillary, mastectomy scar, or other. The other category included patients with different, other, or missing surgical approach. Inframammary was used as the reference category.
- Surgical placement was classified as submuscular, subglandular, subpectoral, or other. For the Augmentation cohort, a subanalysis was performed where the submuscular and subpectoral categories were merged together. These analyses are presented as "A-suffixed" tables in Appendix D. The "other" category combined mixed (different surgical approaches in the same patient), other, and missing surgical placement. Submuscular was used as the reference category.
- Incision size was included in the model as a continuous variable. For bilateral patients, the average of the two incision sizes was used.
- Irrigation solutions used in pocket were classified as saline only, steroid, antibiotic, drug, or other. The "Other" category combined mixed, other, and missing irrigation solutions. Saline only was used as the reference category.
- Surface type was classified as smooth surface, textured surface, or the patient was implanted with one of each surface type. Patients were classified based on the surface type of their implants; bilateral patients with one implant with a smooth surface and one with a textured surface were classified as mixed. Smooth surface was used as the reference category.
- Pooling of study sites was done separately for each indication. Among the Augmentation and Reconstruction cohorts, study sites with fewer than 20 patients were grouped and used as the reference category for analysis by site. Among the Revision cohort, study sites with fewer than 10 patients were grouped.
- Tissue expander use was classified as "Yes" or "No." Patients having a tissue expander prior to implantation were used as the reference category. This variable was included only in the models used for Reconstruction patients.
- Implant size was classified as $\leq$ 349 cc, 350-399 cc, 400-499 cc, 500-599 cc, and $\geq$ 600 cc. Implant size was a continuous variable.

4.5.2 Deaths

Patient deaths during the first 3 years of the study were tabulated cumulatively across visits, regardless of reason, in the patient accounting table.

4.5.3 Rheumatology Assessment

The incidence of rheumatic disease newly diagnosed by a rheumatologist by type of diagnosis; the incidence of patient reported new postoperative potential rheumatologic symptoms; and the incidence of rheumatologic physical examination findings were tabulated. The corresponding cumulative incidences were estimated at 1 year, 2 years, and 3 years using Kaplan-Meier methods in a manner similar to complications and reoperations.

4.5.4 Mammography

For those patients who received mammography testing, the incidence and Kaplan-Meier Cumulative Incidence rate of new postoperative abnormal mammography regardless of biopsy results, and by biopsy result, were analyzed in a manner similar to complications and reoperations.

Any changes in postoperative mammography results relative to preoperative results were tabulated by a standardized system from the American College of Radiology for reporting the results of mammography, Breast Imaging Reporting and Data System, or BIRADS:

0 – Incomplete assessment
1 – Negative
2 - Benign
3 - Probably benign finding
4 - Suspicious abnormally
5 - Highly suggestive of malignancy

BIRADS also includes standard interpretation and reporting formats, a standard dictionary of terms, and standard disease classifications used in checking program effectiveness.

4.5.5 Screening and Detection of Implant Rupture

Ruptures of silicone gel-filled breast implants may be "overt" or "silent," the latter referring to those ruptures that are not clinically evident to the patient or physician without the use of imaging techniques, such as MRI. An estimate of the overall cumulative incidence of rupture must include the occurrence of both overt and silent ruptures. In order to obtain such an estimate for Mentor's Silicone Gel-Filled Breast Implants, a large subset of the Core Gel Study patients was randomly chosen to undergo MRI scans post surgery to detect silent rupture (while overt ruptures, if present in this subset, were identified directly by the study investigators). The MRI scans were conducted at 1 and 2 years post surgery and are to be repeated at 4, 6, 8 and 10 years post surgery. Once completed, these scans were reviewed by a central reviewer blinded to patient identification. The central reviewer is Nanette DeBruhl, M.D., Associate Professor at UCLA School of Medicine, Department of Radiological Sciences. She is an internationally recognized authority in the field of breast imaging and has written numerous publications, as well as chapters in textbooks.[1] The MRI scans were also read by the local radiologist. Further verification of ruptures, identified either directly by study investigators or through MRI screening, was provided through explant and visual examination of retrieved devices by Mentor. Additionally, devices that were explanted for other reasons and returned to Mentor were further evaluated to determine whether undetected rupture was present in these implants.

4.5.5.1 Analysis of Rupture Rate in the MRI Substudy

The rupture rate analysis was conducted using only patients selected for the MRI sample ("MRI substudy"). This sample was a randomly selected subset of the study population, and hence, it is statistically representative of that population. Thus, an estimate of the overall rupture rate based on this sample provides a valid estimate of the overall rupture rate for the entire study population. This sample was used as the basis for estimating the overall rupture rate, as it is only in this sample that both silent ruptures and overt ruptures would have been detected.

In addition to summarizing patient and implant characteristics for patients in the MRI substudy, a Kaplan-Meier survival analysis was performed. The unit of time used for the analysis was 3 years. Only the original study implants were considered in the analysis. Analyses were conducted for each cohort (Augmentation, Reconstruction, Revision, and Overall). Also, all analyses were conducted at the patient level and at the implant level.

The following hierarchy (in descending order) was used to determine whether or not a rupture (including "silent" ruptures) occurred. Specifically, the first available of these listed determinations was used. Determination based on visual examination of the device by Mentor was used whenever available.

1. Determination based on visual examination by Mentor following explantation of the implant.
2. Determination based on physical examination by surgeon following explantation of the implant, as indicated on Adverse Event Case Report Form. Implementation of this aspect of the hierarchy was predicated on the assumption that, upon examination of an explanted device, the surgeon would, if needed, update the AE CRF. Specifically, (1) if a rupture was newly identified upon examination, the rupture would be recorded and (2) if an implant which had been previously recorded as ruptured was determined, upon examination, to be intact, the previously recorded rupture would be deleted.
3. Determination based on MRI findings without explantation of the implant, as indicated on Adverse Event Case Report Form. MRI finding was given precedence over the surgeon's finding (4 below) without explantation, unless the surgeon has a finding of rupture in a year subsequent to the (last) MRI. A device was considered to be ruptured if either the local radiologist or the Central MRI reviewer indicated any of the following:
   - evidence of rupture;
   - evidence of extracapsular silicone;
   - indeterminate for rupture; or
   - indeterminate for extracapsular silicone.

   Subsequently, a suspected rupture was considered to not be ruptured, if a follow up MRI was read by both the local radiologist and the Central Reviewer as not being ruptured, or if upon explant, the device is found to not be ruptured.
4. Determination based on surgeon's findings without explanation of the implant, as indicated on Adverse Event Case Report Form. MRI finding (3 above) was given precedence over the surgeon's finding without explantation unless the surgeon has a finding of rupture in a year subsequent to the (last) MRI.

If, based on the above hierarchy, a rupture was determined to have occurred, the year of occurrence (e.g., year 1, 2 or 3 following implantation) was assigned based on the earliest reporting of a rupture (including "silent" rupture) be it the surgeon's reporting of an overt rupture, an MRI finding of rupture, or as verified by Mentor visual examination of the explanted device. If a rupture was first reported based on a visual examination of the explanted device, the rupture was considered to have occurred in the same year as the year in which the implant was explanted.

In determining year, nominal visit times were used. For example, if a "silent" rupture is diagnosed based on the MRI conducted in the second year after implantation, the rupture was considered to have occurred in year 2.

A patient (implant) was not included in the analysis for a given year if (1) the patient (implant) did not have a rupture in that year and either (2a) the patient did not return for that year's visit or any subsequent visits as of the study data cutoff; (2b) the patient did not undergo their MRI scheduled for that year, or any subsequent MRIs as of the study data cutoff; (2c) the patient had all implants explanted (the implant was explanted) by the time of that year's visit (without evidence of rupture); or (2d) the study data cutoff occurred in that year for the patient.

It should be recognized that the proposed method is biased and is likely to overestimate the overall rate of ruptures to some extent. The bias arises from the fact that a patient who would not be included in the analysis for a given year due to lack of complete follow-up for the year is instead included in the analysis if a rupture occurs and is identified in the study. The extent of such bias increases with the proportion of patients lost to follow-up and the proportion of existing ruptures identified in the study among patients who are, or would otherwise be, lost to follow-up.

4.5.5.2 Rupture among Non-MRI Substudy Patients

Non-MRI substudy patients were evaluated by study investigators for overt ruptures. Only in relatively rare circumstances would the non-MRI substudy patients be expected to receive MRIs during the post surgery follow-up period. As such, ruptures reported among these non-MRI patients would generally include only overt ruptures, and not silent ruptures. It is for this reason that the determination of the cumulative incidence of overall rupture of Mentor's silicone gel-filled breast implants, as described above, is based directly on MRI substudy patients, who have been screened for both silent and overt rupture.

4.6 Effectiveness

The primary effectiveness endpoint was assessed based primarily on changes in chest circumference and bra cup size (Augmentation cohort only). Secondary effectiveness was based on changes in the Quality of Life questionnaire and global patient satisfaction.

4.6.1 Primary Effectiveness Endpoint – Circumferential Chest Size and Bra Cup Size

Overall mean changes from preoperative assessments and standard deviations of changes were calculated for selected variables. The overall mean change from preoperative assessment was calculated by obtaining for each patient her average change from the preoperative assessment across all available scheduled postoperative assessments and then calculating the mean across patients of these averages. A Wilcoxon signed rank test was performed on the overall mean change in order to assess the statistical significance of the change from the preoperative assessment. For circumferential chest size and bra-cup size assessment a Wilcoxon signed rank test was also performed on the change from the preoperative assessment to the Year 3 visit.

Patient analyses are presented for Augmentation patients, Reconstruction patients (limited to delayed post-mastectomy), Revision patients, and patients overall. Analyses are also presented by device placement (submuscular, subglandular, and subpectoral) within patient cohorts (Augmentation, Reconstruction, Revision, overall) for the Tennessee Self-Concept Scale, Body Esteem Scale and the Rosenberg Self-Esteem Scale.

For immediate post-mastectomy patients inferential analyses on overall mean change from baseline were not performed. This is because the baseline measurements for these patients were prior to mastectomy and consequently the patients never experienced a post-mastectomy condition without an implant. Descriptive statistics at each visit and relative to preoperative assessments were, however, presented for this group.

For the reason cited above, analyses of effectiveness data for the overall and Reconstruction overall groups excluded data for immediate post-mastectomy patients.

4.6.1.1 Circumferential Chest Size

Summary statistics of circumferential chest size were tabulated for baseline and postoperative visits. The overall mean change and standard deviation of change in circumferential chest size was calculated. The circumferential measurement was taken by measuring the circumference of the chest at the nipple level. If the nipple was absent, the measurement was made at the level where the nipple would have been located.

4.6.1.2 Bra-Cup Size

Bra-cup size change from baseline was summarized at the patient level for each follow-up visit. The overall average number of steps of bra-cup size increase was calculated (a one-step increase is from A to B; a two-step increase is from A to C, etc.). An analysis of bra-cup size was only performed for Augmentation patients. If the measurements recorded for right and left breast were different for a particular visit the following algorithm was used:

- *If the difference between the right and left breasts was two sizes or greater:* If the difference between the right and left breasts was two sizes or greater then the average of the two measurements (rounded down) was used for analyses (e.g., if one breast is A and the other is C or if one breast is A and the other is D then B was used in analyses).
- *If the difference between the right and left breasts was one size:* If the difference between the right and left breasts was only one size, then the value of the smaller breast was used in analyses (e.g., if A and B then A used in analyses).

4.6.2 Second Effectiveness Endpoint - Quality of Life

Quality of Life assessments were used as secondary endpoints of effectiveness. These validated instruments included: the Tennessee Self-concept Scale (TSCS), the SF-36 Health Survey Scale, the Body Esteem Scale, the Rosenberg Self-Esteem Scale, the Manitoba Cancer Treatment & Research Foundation Functional Living Index: Cancer (FLIC) (cancer patients only), and Global Patient Satisfaction.

Except for the SF-36 Health Survey Scale, if a patient was missing any items of the scale, then the patient's visit with the missing items was excluded from analysis. For the SF-36 Health Survey Scale, if a subscale was missing an item, then means of the items in the subscale for that patient were used to impute the missing value. This was only done if fewer than one-half of the items in the subscale were missing.

4.6.2.1 The Tennessee Self-concept Scale (TSCS)

The Tennessee Self Concept Scale (TSCS) consists of 100 self-descriptive items that allow an individual to portray what he or she is, does, likes, and feels. The TSCS is scored on a 5 point scale, ranging from completely true to completely false. The scale is intended to summarize an individual's feeling of self-worth, the degree to which the self-image is realistic, and whether or not that self-image is a deviant one. As well as providing an overall assessment of self-esteem, the TSCS measures five external aspects of self-concept (moral-ethical, social, personal, physical, and family) and three internal aspects (identity, behavior, and self-satisfaction). In addition, crossing the internal and external dimensions results in the mapping of 15 "facets" of self-concept.[2]

4.6.2.2 Short Form 36 (SF-36)

The SF-36 was designed for use in clinical practice and research, health policy evaluations, and general population surveys. It is a multi-purpose, short-form health survey with 36 questions. The SF-36 yields an 8-scale profile of functional health and well-being scores as well as psychometrically based summary measures – the Physical Component Score (PCS) and Mental Component Score (MCS). It is a generic measure, as opposed to one that targets a specific age, disease, or treatment group. The SF-36 is suitable for self-administration, computerized administration, or administration by a trained interviewer in person or by telephone, to persons age 14 and older. It can be administered in 5-10 minutes.[3]

The interpretation of results has been simplified with the standardization of mean scores and standard deviations for all SF-36 scales. Specifically, norm-based scoring has proven to be very useful when interpreting differences across scales in the SF-36 profile and for monitoring disease groups over time.

4.6.2.3 Body Esteem Scale (BES)

The BES is a factorially derived measure of female body esteem. This assessment contains questions related to 35 individual body parts and functions; for example, "How do you feel about the appearance of your buttocks?" For women, three subscales measure sexual attractiveness, weight concern, and physical condition. Items are rated on a five-point Likert scale ranging from strong negative feelings to have strong positive feelings.[4]

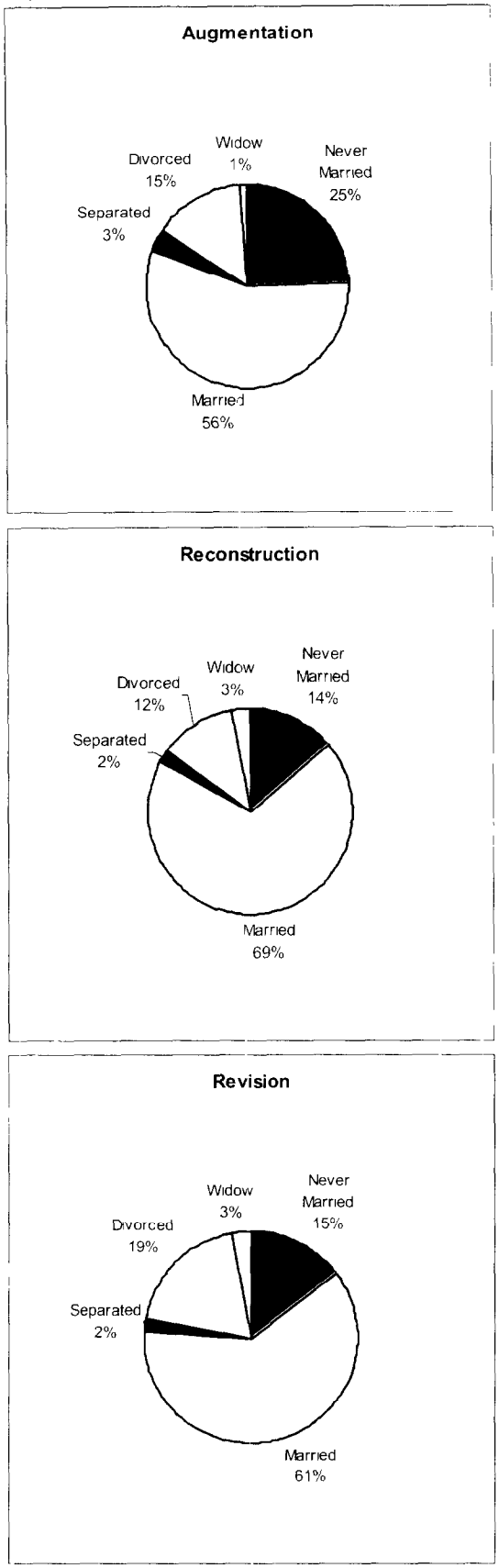
4.6.2.4 Rosenberg Self-Esteem Scale (SES)

The Rosenberg SES is a 10-item self-report measure of global self-esteem. It consists of 10 statements related to overall feelings of self-worth or self-acceptance. The items are answered on a four-point scale ranging from strongly agrees to strongly disagree. The Rosenberg Self-Esteem Scale was developed to assess global and unidimensional self-esteem. Ratings are assigned to all the items after reverse scoring the positively worded items. Scores range from 10 to 40, with higher scores indicating higher self-esteem.[5,6]

4.6.2.5 Manitoba Cancer Treatment & Research Foundation Functional Living Index: Cancer (FLIC)

The Functional Living Index-Cancer (FLIC) is a subjective tool developed for use in clinical trials. This 22-item self-report questionnaire is designed for ease of administration. Items are presented in a Likert-like format on a scale of 1 to 7. Subscales assess physical well-being, psychologic state, family situational interaction, social ability, and somatic sensation.[7] This scale was suitable only for the delayed post-mastectomy reconstruction patients.

Figure 5.2.2-A: Marital Status



5.2.3 Physical Exam and Medical History

Of the overall study population, 26% of the patients were former smokers and 16% were current smokers. Within each body system examined at baseline, greater than 95% of the women had no abnormality.

Seventy-three percent of women overall had at least one prior surgery (exclusive of surgery for cancer), including for example, cesarean section, appendectomy, hysterectomy, and liposuction. Preexisting medical conditions included allergies (45%), history of neurological disease (12%), including depression, migraine headache, and attention deficit disorder, and prior cardiovascular disease (11%).

5.3 Implant and Operative Characteristics

Sixty-two percent of the implants had a smooth surface. The average incision size was 5.3, 4.3, 7.2, and 5.6 cm for the Overall patient population, Augmentation, Reconstruction, and Revision cohorts, respectively. Most of the patients had a concurrent surgery at the time of breast implantation, including lipoplasty, mastopexy, and blepharoplasty.

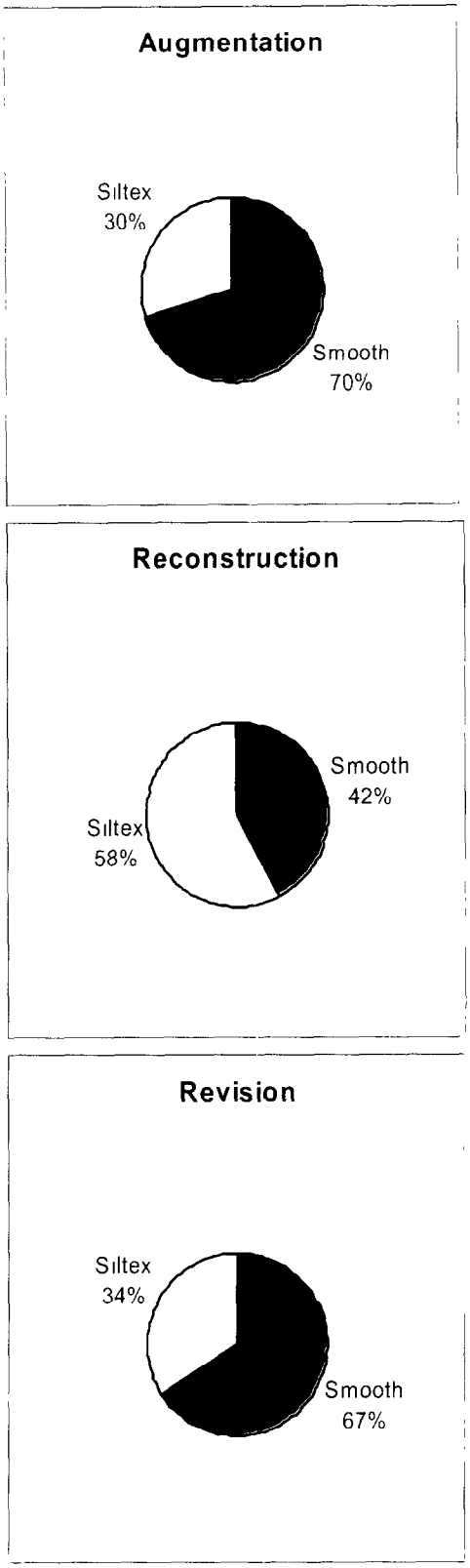
In the Augmentation cohort, inframammary (59%), was the most common surgical approach. Mastectomy scar (56%) was the most common surgical approach for the Reconstruction cohort, and inframammary (61%) for the Revision cohort. Submuscular was the most common surgical placement for all cohorts (42%, 61%, 54% for Augmentation, Reconstruction, and Revision, respectively).

Fifty-five percent of all patients received antibiotics as part of operative pocket irrigation; 40% received saline only; and 8% received steroids with and without antibiotics. Note that as more than one category could have been selected, the total does not equal 100%.

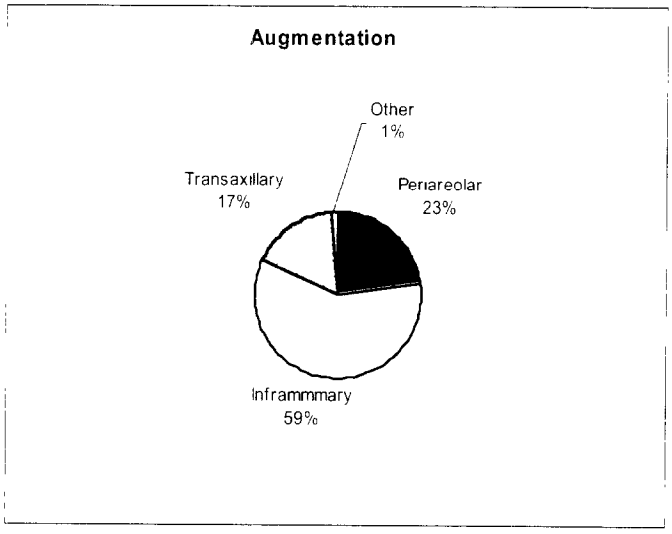
During the initial implant surgery, four of the devices were inadvertently damaged by the surgical team during placement. All patients were implanted with another Core device and continue to be followed in the study.

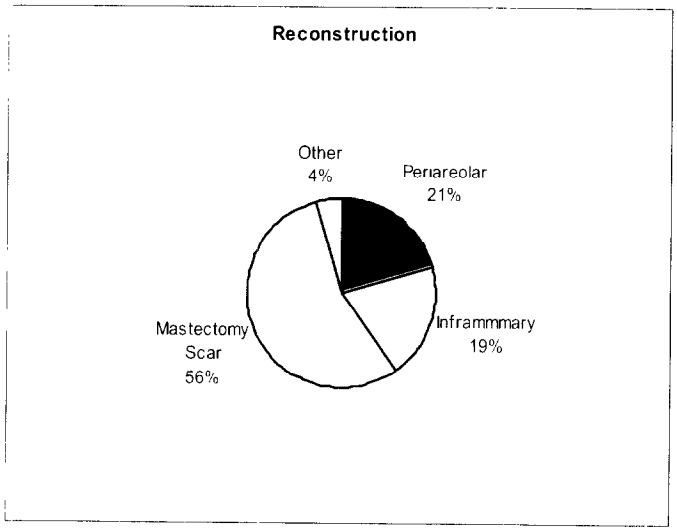
Surface texturing is summarized in Figure 5.3-A below. Surgical approach and placement are summarized in Figures 5.3-B and 5.3-C, respectively. Appendix D Table 7 contains full details on the operative characteristics associated with the initial mammoplasty procedure for each breast.

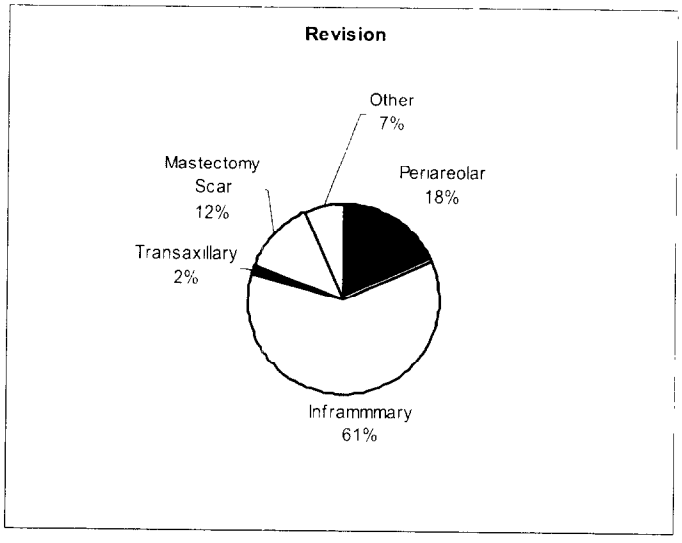
Figure 5.3-A: Surface Texturing by Indication



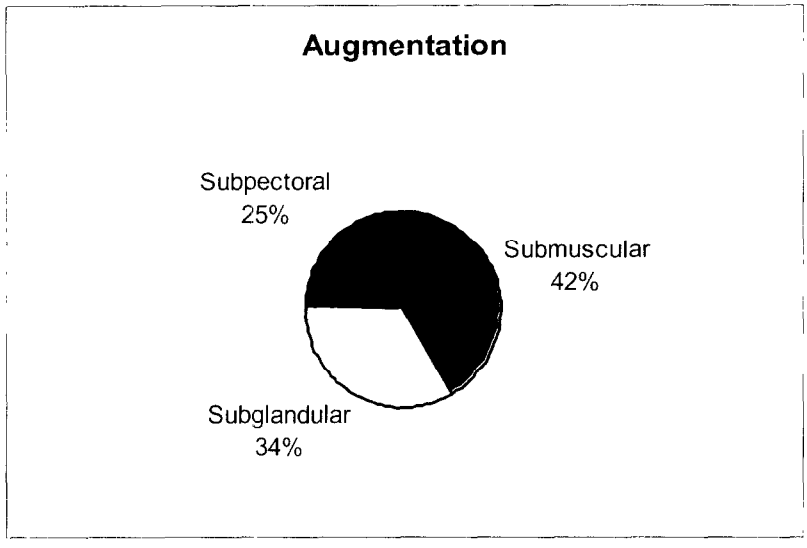
5.3-B: Surgical Approach

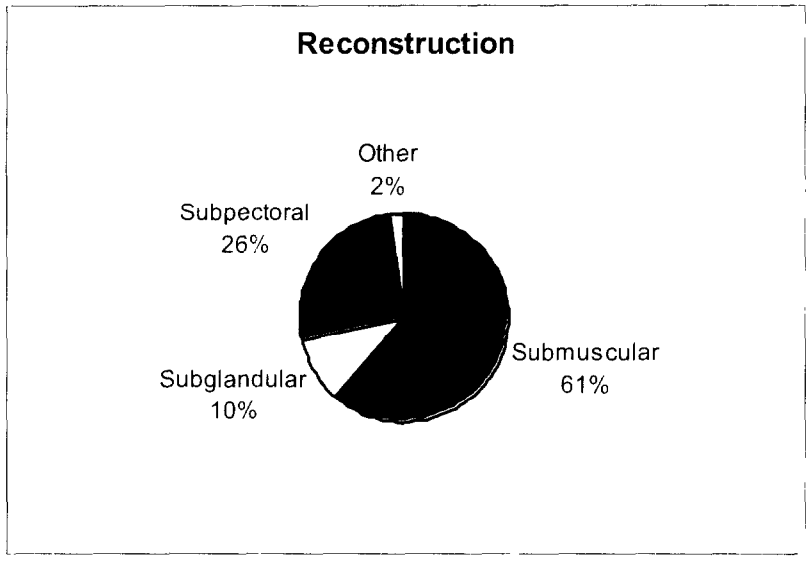






5.3-C: Surgical Placement





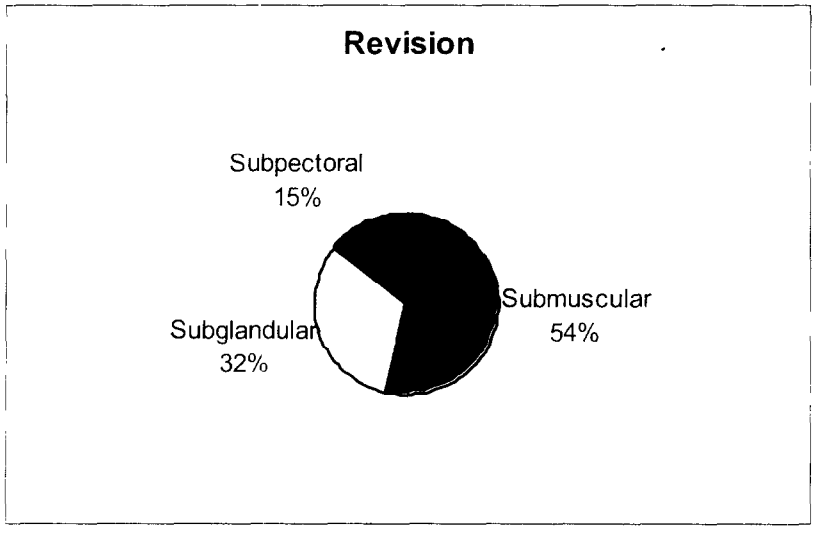
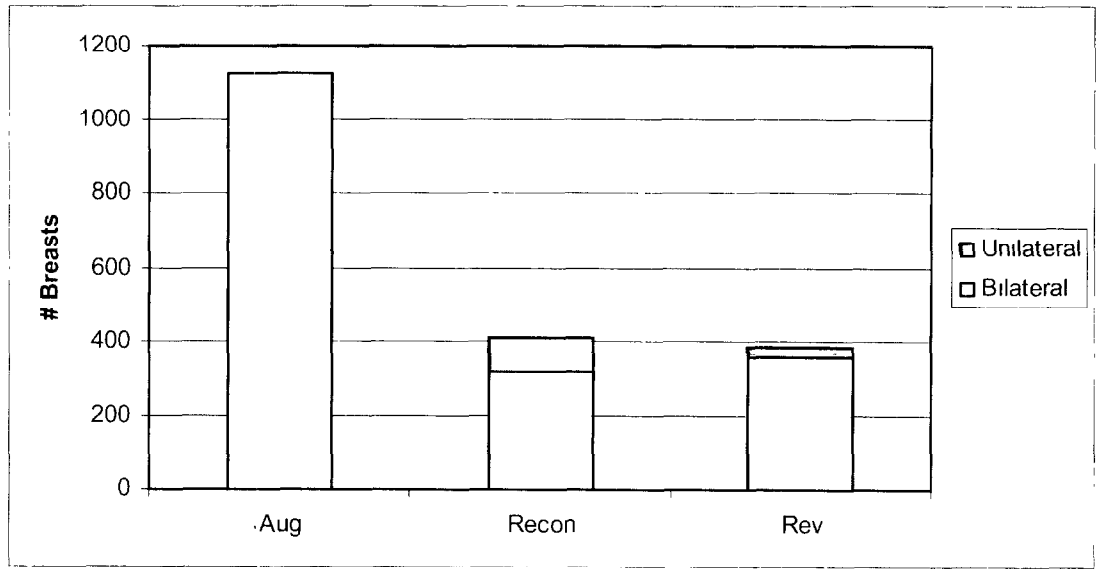


Figure 5.3-D: Unilateral and Bilateral



5.4 Safety

Complications are presented by individual event, and by cosmetic or non-cosmetic events defined as follows:

- *Cosmetic:* asymmetry, hypertrophic scarring, ptosis, patient requested size change, and wrinkling
- *Non-cosmetic:* Baker III or Baker IV capsular contracture, breast pain not associated with any other complication, nipple and breast sensation changes, calcification, delayed wound healing, extrusion, granuloma, hematoma, infection, lymphadenopathy, necrosis, new diagnosis of breast cancer or rheumatic disease, position change, rupture, seroma, and lactation difficulties.

The complication rates do not include the planned second stage procedures of nipple reconstruction and nipple tattooing.

It also should be noted that all surgical procedures have a small risk of complication inherent to the surgery itself and to anesthesia. These complications include infection, hematoma, seroma, scarring, and those related to anesthesia.

The safety analysis performed included:

- Analysis of complications by Kaplan-Meier Cumulative Incidence Rate
- Severity, treatment, and resolution of complications
- Reoperations and explants
- Complications after reimplantation
- Prevalence and incidence of complications
- Cox regression
- Deaths
- Reproduction and lactation complications
- Breast cancer complications
- Connective tissue/autoimmune/rheumatology disease complications
- Mammography
- Rupture, Possible Rupture, Extracapsular Silicone Gel, and the MRI Substudy

5.4.1 Kaplan-Meier Cumulative Incidence Rates for Postoperative Complications and Reoperations through 3 Years

The Augmentation 3-year Kaplan-Meier Cumulative Incidence rate for the following key non-cosmetic complications were: rupture 0.2%, capsular contracture III/IV 8.2%, infection 1.5%, explantation with replacement 2.9%, explantation without replacement 2.5%, and any reoperation 15.0%. Cumulative Kaplan-Meier cumulative confidence rates for these complications are summarized by cohort in Table 5.4.1-A,B, and C and Figure 5.4.1-A below. Kaplan Meier survival curves are provided for capsular contracture, infection, reoperation, explantation, and rupture in Figures 5.4.1-C through 5.4.1-G, respectively.

The Reconstruction 3-year Kaplan-Meier Cumulative Incidence rate for the following key non-cosmetic complications were: rupture 0.6%, capsular contracture III/IV 8.8%, infection 5.3%, explantation with replacement 7.4%, explantation without replacement 62%, and any reoperation 26.3%.

The Revision 3-year Kaplan-Meier Cumulative Incidence rate for the following key non-cosmetic complications were: rupture 3.7%, capsular contracture III/IV 17.2%, infection 1.0%, explantation with replacement 7.5%, explantation without replacement 6.0%, and any reoperation 26.3%.

The Kaplan-Meier Cumulative Incidence rate of reoperation for each of the three cohorts is 15.0%, 26.3%, and 26.3% for Augmentation, Reconstruction, and Revision, respectively. As detailed in Section 5.6.3.1, at 3 years postoperative, 97% of the patients indicated they would have the surgery again. When considering patients who had reoperations, the percentage who indicated that they would have the surgery again was 96%, despite the need for reoperations.

Table 5.4.1-D and Figure 5.4.1-B summarize the cosmetic Kaplan-Meier cumulative confidence rates for the cosmetic complications.

Kaplan-Meier Cumulative Incidence rates of all complications are detailed in Appendix D Tables 8.7.1 and 8.7.2; whereas non-cumulative incidence rates are presented in Appendix D Tables 8.1 through 18.7. All levels of severity are included in these analyses, except for milf occurrences of the following: asymmetry, breast pain, calcification, implant malposition/displacement, nipple sensation changes, breast sensation changes, nipple complications, and wrinkling.

Table 5.4.1-A: 3-year Kaplan-Meier Cumulative Incidence Rates of Occurrence of Key Complications. Augmentation N=551

Key Complications	Patient		Implant	
	%	CI	%	CI
Rupture	0.2	0,0.7	0.1	0,0.3
Capsular contracture III/IV	8.2	5.9,10.6	5.6	4.2,7.0
Infection	1.5	0.5,2.5	0.7	0.2,1.2
Explant with replacement	2.9	1.4,4.3	2.3	1.4,3.2
Explant without replacement	2.1	1.1,3.9	21	1.2,3.0
Reoperations >1%				
Any Reoperations	15.0	11.9,18.0	10.5	8.7,12.4
Capsulectomy	4.6	2.8,6.5	2.9	1.9,4.0
Capsulotomy	2.3	1.0,3.6	1.5	0.8,2.2
Incision and Drainage	2.0	0.8,3.2	0.9	0.4,1.6
Scar revision	2.3	1.0,3.6	1.7	0.9,2.5
Complications ≥ 1%				
Breast mass	2.4	1.0,3.7	1.3	0.6,2.0
Breast pain	1.7	0.6,2.8	1.3	0.6,1.9
Breast sensation changes	2.2	1.0,3.4	1.6	0.9,2.3
External injury not related to implant	1.4	0.2,2.6	0.8	0.2,1.4
Hematoma	2.6	1.2,3.9	1.3	0.6,1.9
Miscarriage	1.4	0.4,2.4	NA	NA
Nipple sensation changes	10.8	8.1,13.4	8.2	6.6,9.9

Table 5.4.1-B: 3-Year Kaplan-Meier Cumulative Incidence Rates of Occurrence of Key Complications. Reconstruction N=251

Key Complication	Patient		Implant	
	%	CI	%	CI
Rupture	0.6	0,1.8	0.4	0,1.2
Capsular contracture III/IV	8.8	4.0, 12.7	6.2	3.6,8.9
Infection	5.3	2.5,8.1	3.5	1.6,5.3
Explant with replacement	7.4	4.1,10.8	6.2	3.7,8.6
Explant without replacement	6.2	2.8,9.7	5.6	2.9, 8.3
Reoperations >1%				
Any Reoperation	26.3	20.7,31.9	21.4	17.2,25.5
Biopsy	3.4	1.1,5.7	2.2	0.7,3.7
Capsulectomy	3.8	1.4,6.3	3.0	1.3,4.5
Capsulorraphy	0.8	0,1.9	0.5	0,1.3
Capsulotomy	5.4	2.5,8.2	3.8	1.8,5.7
Implant pocket revision	1.7	0,3.4	1.7	0.3,3.0
Implant reposition	5.0	2.3,7.8	4.1	2.1,6.1
Incision and Drainage	2.1	0,4.2	1.3	0,2.7
Scar revision	2.2	0.3,4.0	2.0	0.5,3.4
Skin adjustment	4.1	1.6,6.7	3.8	1.8,5.7
Complications ≥ 1%				
Breast mass	3.9	1.1,6.6	2.2	0.5,3.9
Breast pain	1.7	0,3.4	1.1	0,2.2
Extrusion	1.2	0,2.6	0.8	0,1.7
Hematoma	1.5	0,3.3	1.0	0,2.1
Implant malposition/displacement	1.7	0,3.3	1.4	0.2,2.6
Lymphadenopathy	1.7	0,5.1	1.2	0,3.4
Metastatic disease	1.9	0,3.7	2.6	0,6.2
Necrosis	1.2	0,3.1	0.8	0,1.9
Nipple sensation changes	3.1	0,6.3	2	0,4.1
Recurrent breast cancer	1.7	0,3.4	1.1	0,2.2
Seroma	4.9	2.2,7.6	3.2	1.4,4.9

Table 5.4.1-C: 3-Year Kaplan-Meier Cumulative Incidence Rates of Occurrence of Key Complications. Revision N=205

Complication	Patient		Implant	
	%	CI	%	CI
Rupture	3.7	0.8,6.7	2.0	0.4,3.6
Capsular contracture III/IV	17.2	11.9,22.4	12.3	8.9,15.7
Infection	1.0	0,2.4	0.6	0, 1.3
Explant with replacement	7.5	3.7,11.4	6.1	3.5,8.6
Explant without replacement	6.0	2.5,9.4	5.3	2.9,7.7
Reoperation >1%				
Any Reoperation	26.3	20.0,32.6	21.3	17.0,25.6
Biopsy	3.7	1.0,6.5	2.0	0.5,3.5
Capsulectomy	6.4	2.8,9.9	4.7	2.4,7.0
Capsulorraphy	1.0	0,2.4	1.1	0,2.1
Capsulotomy	5.7	2.4,9.0	3.9	1.9,5.9
Implant reposition	2.7	0.3,5.2	3.0	1.1,4.8
Incision and Drainage	2.5	0.3,4.6	1.6	0.3,2.8
Mastopexy	1.7	0,3.7	1.5	0.2,2.7
Scar revision	3.2	0.7,5.8	2.6	0.9,4.2
Skin Adjustment	3.5	1.0,6.1	3.0	1.2,4.7
Complications > 1%				
Breast mass	5.8	2.5,9.1	3.1	1.3,4.9
Breast pain	2.0	0,4.0	1.4	0.2,2.6
Breast sensation changes	2.1	0,4.2	1.4	0.2,2.6
Delayed wound healing	2.0	0,3.9	1.3	0.2,2.5
External injury not related to implant	1.2	0,3.0	0.7	0,1.6
Extrusion	1.5	0,3.1	0.8	0,1.7
Granuloma	1.0	0,2.3	0.5	0,1.3
Hematoma	3.0	0.6,5.3	1.9	0.5,3.2
Implant malposition/displacement	2.5	0.3,4.7	1.9	0.5,3.3
Inflammation	1.5	0,3.2	0.5	0,1.3
Nipple sensation changes	8.6	4.7,12.6	6.7	4.2,9.3
Seroma	2.0	0,3.9	1.1	0,2.1

Figure 5.4.1-A: 3-Year Kaplan-Meier Cumulative Incidence Rates of Occurrence of Non-Cosmetic Key Complications. Overall N=1,007

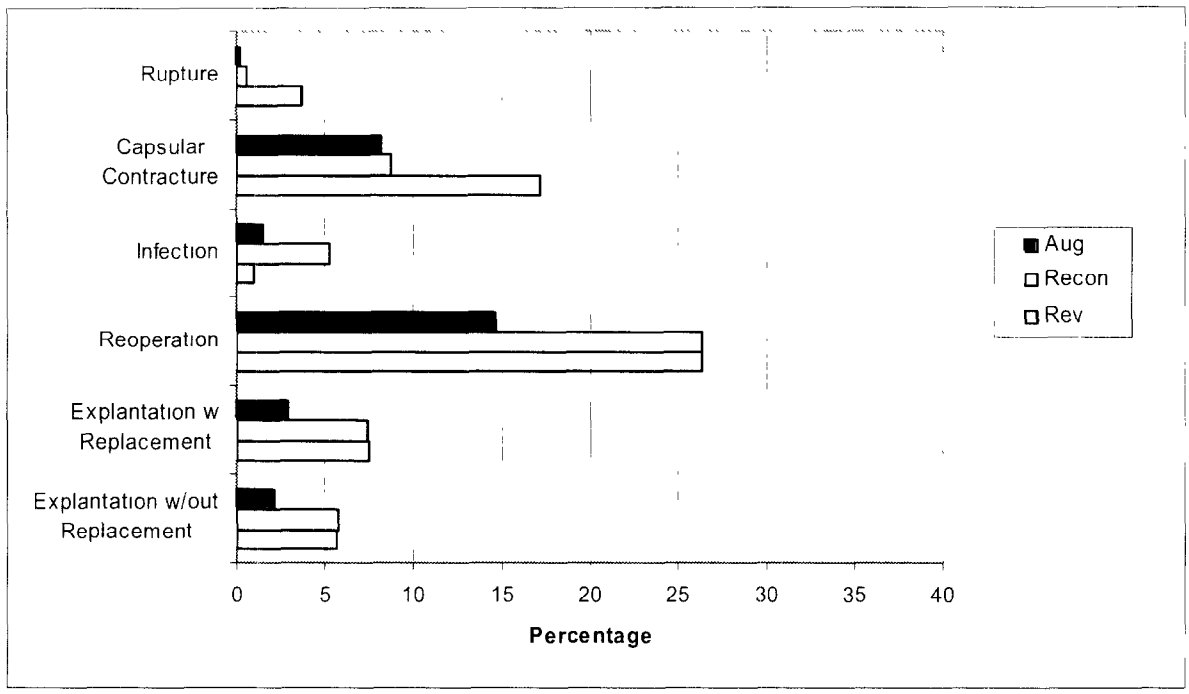


Table 5.4.1-D: 3-Year Kaplan-Meier Cumulative Incidence Rates of Occurrence for Cosmetic Complications

Cohort	Complication*	Patient		Implant	
		%	CI	%	CI
Augmentation N=551 patients	Asymmetry	0.5	0,1.2	0.4	0,0.7
	Hypertrophic Scarring	6.3	4.2,8.3	4.8	3.5,6.1
	Ptosis	2.2	0.9,3.4	2.0	0,2.9
	Wrinkling	0.7	0,1.5	0.5	0,1.0
Reconstruction N=251 patients	Asymmetry	7.1	3.2,11.1	5.6	2.7,8.5
	Hypertrophic Scarring	6.4	3.0,9.8	4.6	2.3,7.0
	Ptosis	6.9	2.0,11.8	5.9	0,9.6
	Wrinkling	2.8	0.5,5.1	2.3	0.7,4.0
Revision N=205 patients	Asymmetry	2.7	0.3.5.1	1.5	0.2,2.7
	Hypertrophic Scarring	6.0	2.7,9.3	5.1	2.9,7.4
	Ptosis	2.2	0,4.3	2.1	0.5,3.6
	Wrinkling	2.0	0,4.0	1.3	0.2,2.5

* Includes moderate or greater levels of asymmetry and wrinkling

Figure 5.4.1-B: 3-Year Kaplan-Meier Cumulative Incidence Rates of Occurrence for Cosmetic Complications. Overall N = 1,007

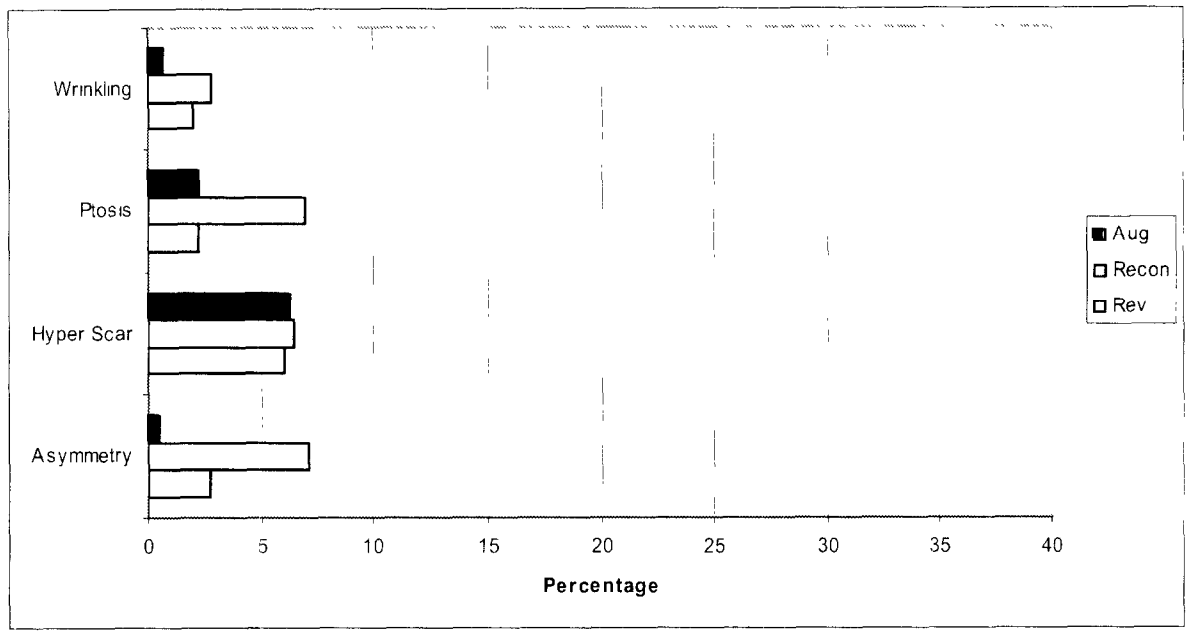


Figure 5.4.1-C: 3-Year Kaplan-Meier Curve for Capsular Contracture, Baker Grade III and IV. Overall N = 1,007

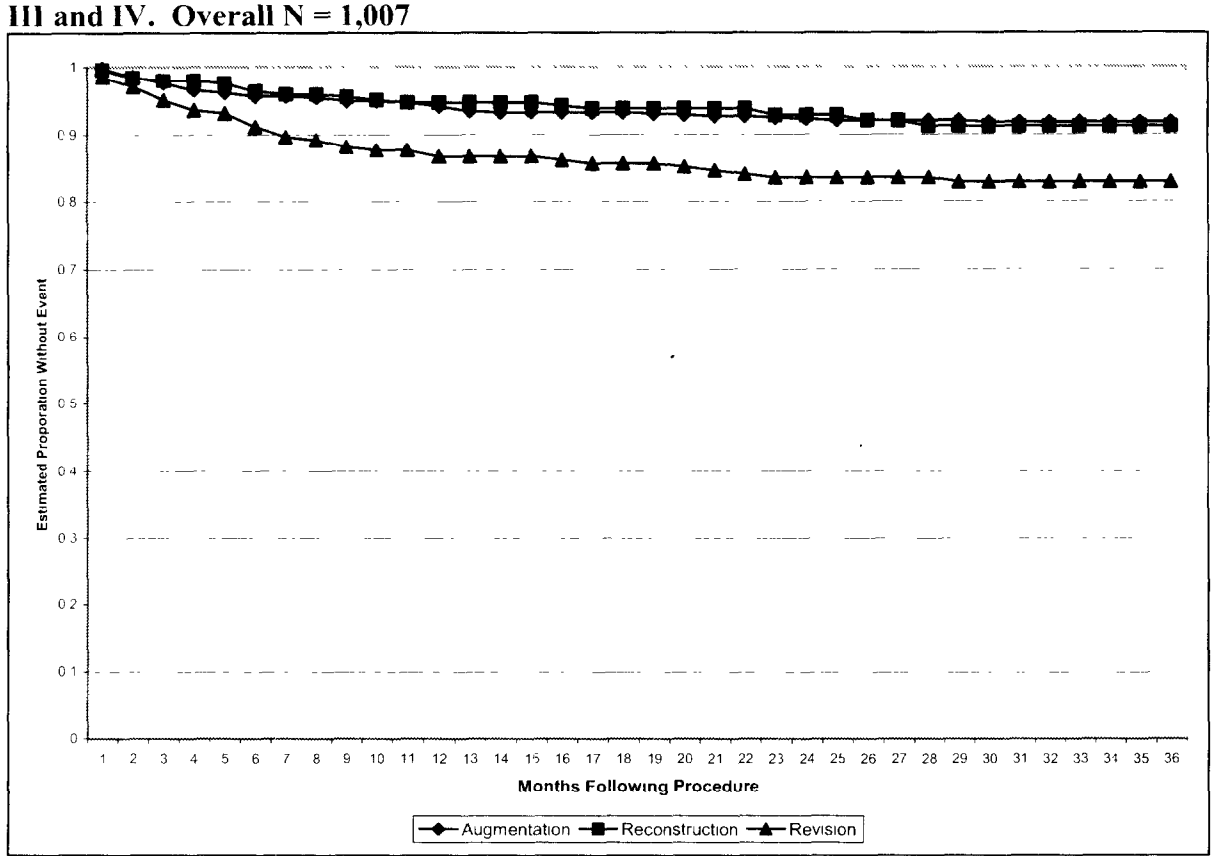


Figure 5.4.1-D: 3-Year Kaplan-Meier Curve for Infection. Overall N = 1,007

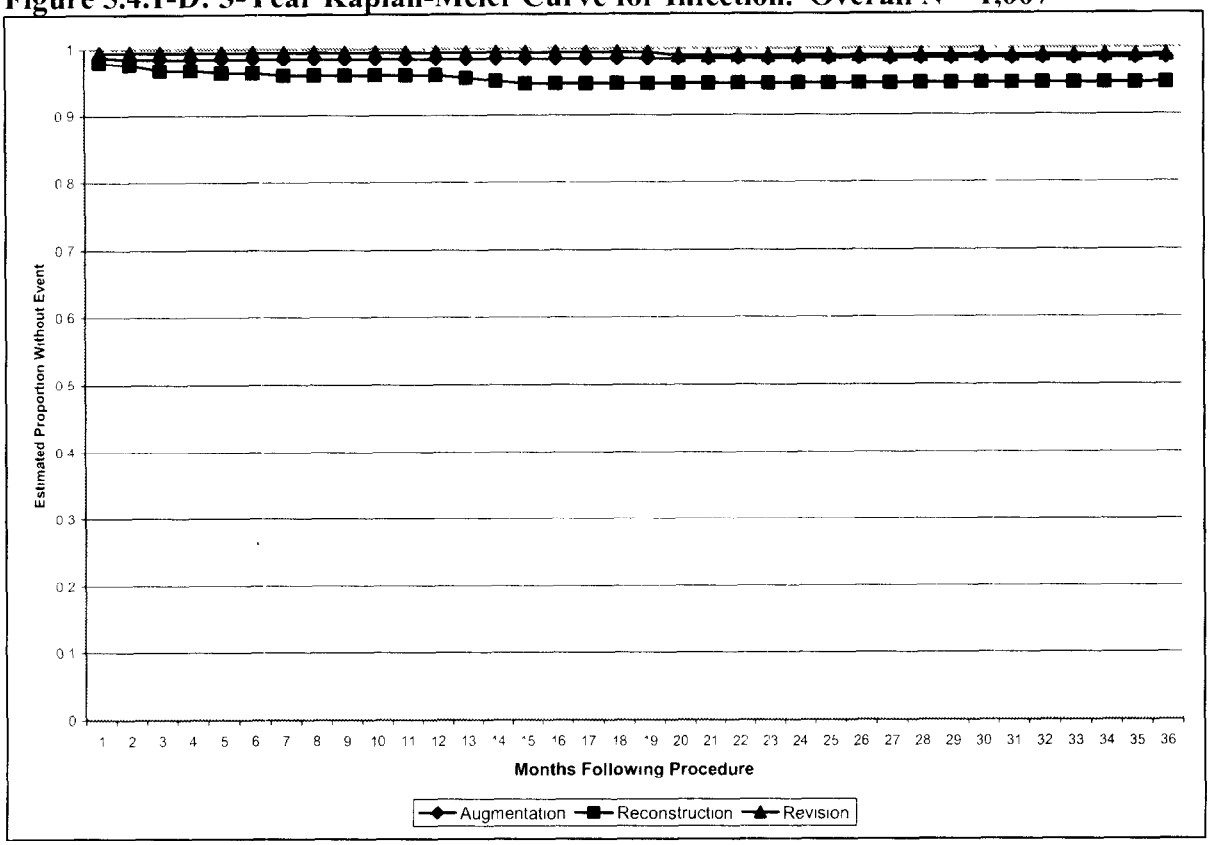


Figure 5.4.1-E: 3-Year Kaplan-Meier Curve for Reoperation. Overall N = 1,007

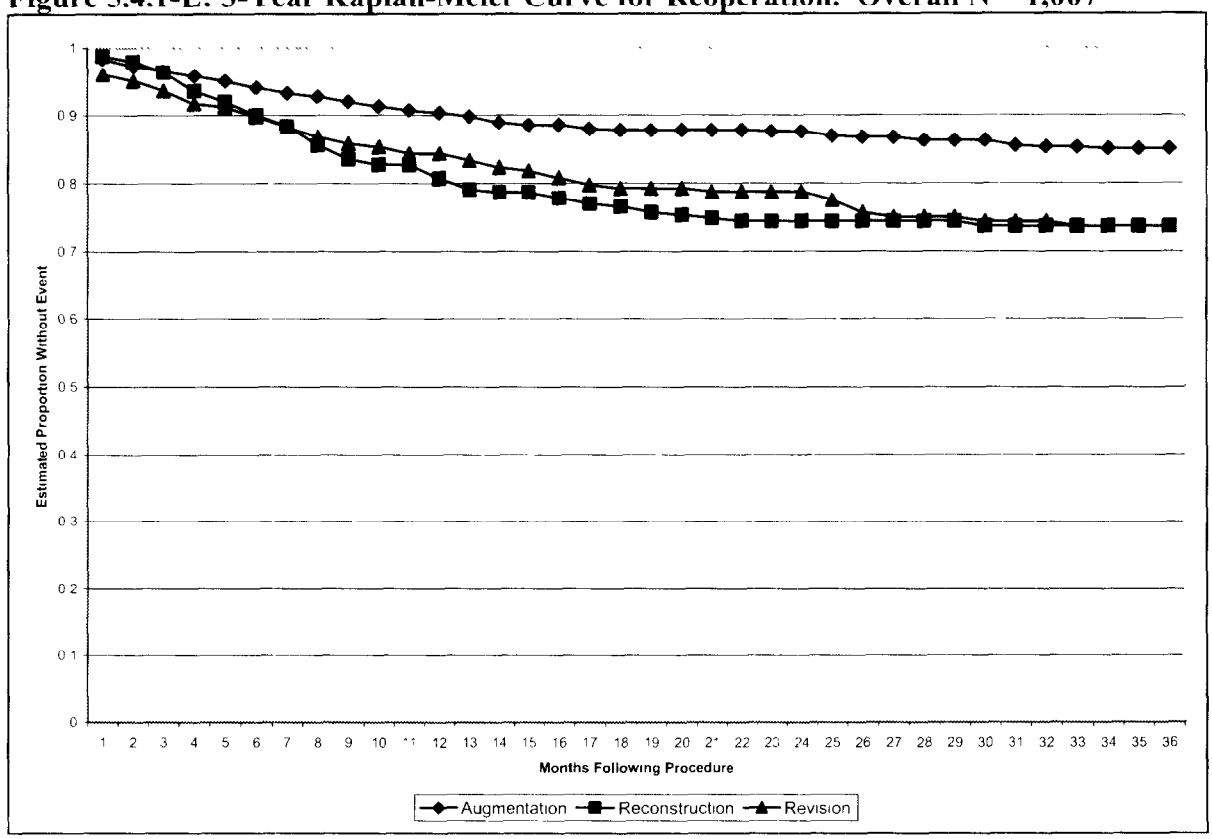


Figure 5.4.1-F: 3-Year Kaplan-Meier Curve for Explant, with and without Removal. Overall N = 1,007

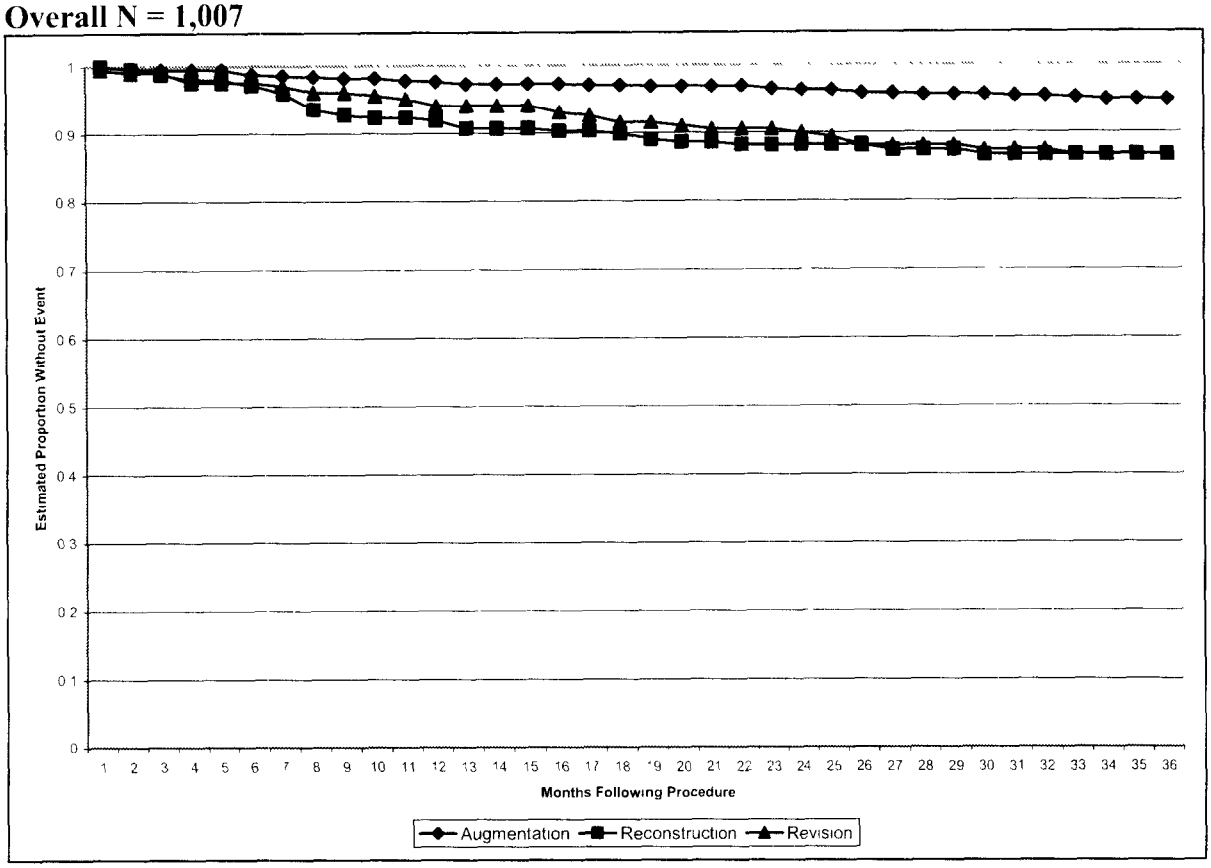
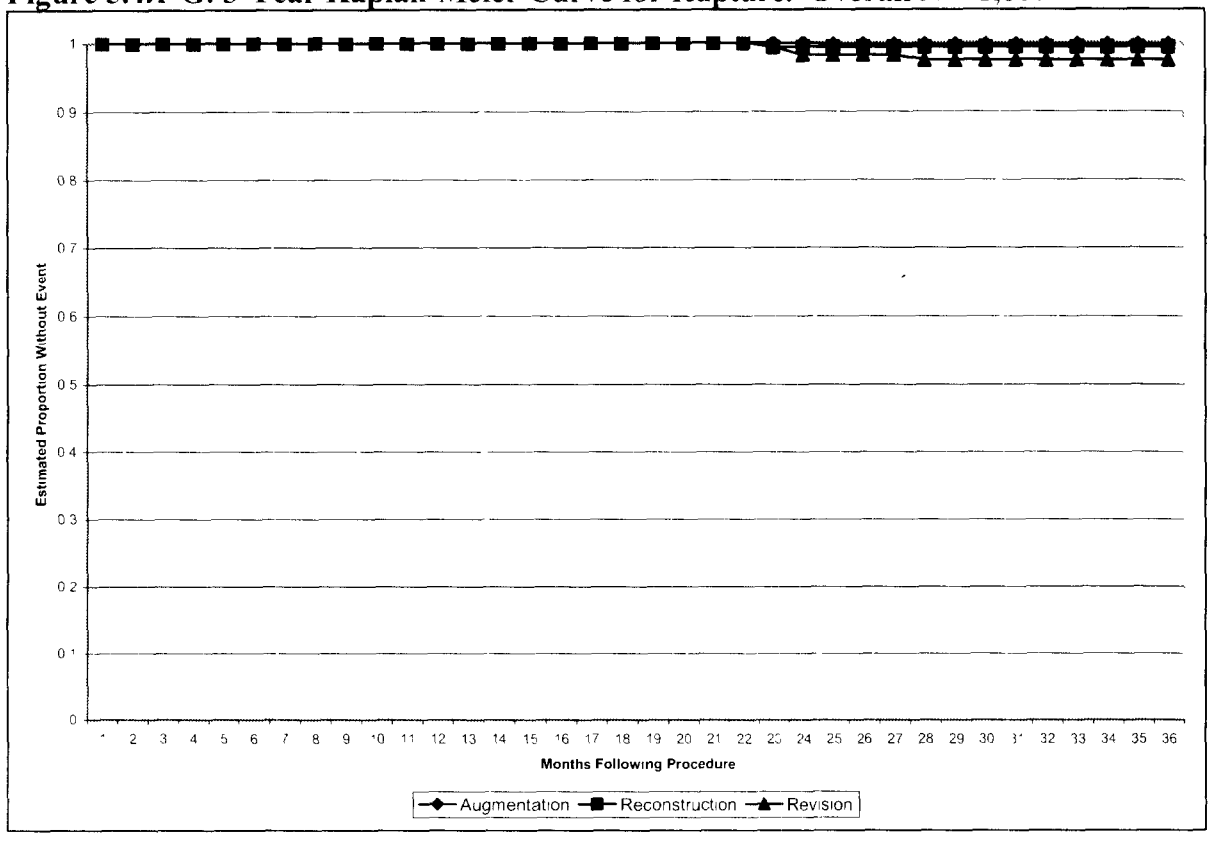


Figure 5.4.1-G: 3-Year Kaplan-Meier Curve for Rupture. Overall N = 1,007



5.4.2 Treatment Required to Resolve Complications

For the overall patient population, more than 33% of the complications resolved without any type of treatment. Of those complications that required treatment, 17% were resolved using medication. Over 97% of the complications were resolved without the need for hospitalization. Of those that required hospitalization, 6 of the 8 patients were in the Reconstruction or Revision cohorts; the remaining 2 patients were Augmentation. Table 5.4.2-A summarizes the methods of resolution by cohort. Appendix D Table 8.4.1 details complication resolution.

Table 5.4.2-A: Treatment to Resolve Complications

	Method of Resolution									
	Without Treatment		Medication		Secondary Procedure		Hospitali - zation		Other	
Complication	n	%	n	%	n	%	n	%	N	%
Augmentation N= 187	71	38.0	38	20.3	60	32.1	2	1.1	15	8.0
Reconstruction N= 102	29	28.4	11	10.8	50	49.0	3	2.9	8	7.8
Revision N= 87	27	31.0	13	14.9	37	42.5	3	3.4	5	5.7

5.4.3 Time to Resolution

For non-cosmetic complications over 69% had been resolved by 3 years. Table 5.4.3-A summarizes the percentage of patients whose complication had resolved by the time of database lock.

Appendix D Table 8.3.1 details resolution status for all cosmetic and non-cosmetic complications.

Table 5.4.3-A: Time to Resolution by Patient through 3 Years. Overall. N=1,007

Complications*	Patients with Complication	Resolved (%)
Breast Mass	31	52
Breast pain	17	88
Breast sensation changes	18	67
Capsular contracture III/IV	97	73
External injury not related to implant	9	78
Hematoma	23	100
Implant malposition/displacement	10	60
Infection	23	96
Miscarriage	9	100
Nipple sensation changes	79	73
Rupture**	8	13
Seroma	21	100

*Only complications with overall Kaplan Meier rates greater than or equal to 1% are listed

** Only if a rupture is explanted, is it considered resolved. Otherwise, it is considered

5.4.4 Reoperations through 3 Years

All analyses are presented on both a patient and implant level, in addition to being presented on an event level, where applicable. Any reoperations performed only for the staged reconstruction procedures of nipple tattooing and nipple reconstruction are not included in the reoperation analysis. The Investigator was required to select one primary reason for the reoperation.

5.4.4.1 Primary Reason for Reoperation through 2 years

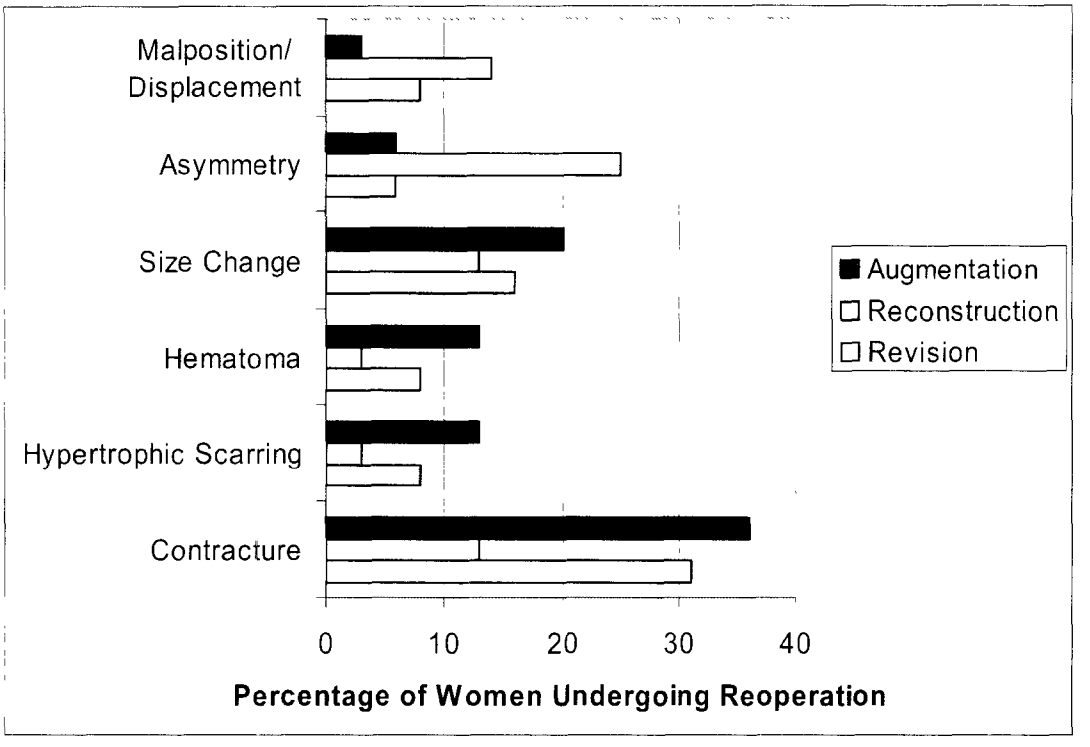
Among the 79 women in the Augmentation cohort who had reoperations, the most frequently reported primary reasons for reoperations were: capsular contracture Baker Class III/IV with 28 patients (35%, 28/79), patient request: 15 patients (19.0%), hematoma: 10 patients (13%), and hypertrophic scarring: 10 patients (13%). Reasons for reoperations are summarized in Figure 5.4.4.1-A below. All other reasons for reoperations occurred in fewer than 10% of patients having a reoperation.

Among the 64 women in the Reconstruction cohort who had reoperations, the most frequently reported primary reasons were: asymmetry with 16 patients (25%, 16/64), implant malposition/displacement: 9 patients (14%), patient request: 8 patients (13%), and capsular contracture Baker Class III/IV: 8 patients (13%). For those patients who had reoperation for capsular contracture, 3/7 of them had prior radiation treatment for breast cancer. Asymmetry, the most frequent reason for reoperation, is cosmetic in nature and is to balance the contralateral breast to the reconstructed breast, and is inherent to any method of breast reconstruction surgery, irrespective of whether autologous tissue or implants are used.

Among the 51 women in the Revision cohort who had reoperations, the most frequently reported primary reasons were: capsular contracture Baker Class III/IV with 16 patients (31%, 16/51), and implant size change 8 (16%)

Full details on reasons for reoperations are provided in Appendix D Table 9.2.

Figure 5.4.4.1-D: Primary Reason for Reoperation by Patient, where Rate is Greater than 10%



5.4.4.2 Types of Additional Surgical Procedures through 3 Years

Among the 551 women in the Augmentation cohort, 79 women (14%, 79/551) had 134 reoperations involving 115 implants, and 160 additional surgical procedures. By patient, the most frequently reported additional surgical procedures were: capsulectomy 24 patients (30%), capsulotomy: 12 patients (15%), implant removal without replacement: 12 patients (15%), implant removal with replacement: 15 patients (19%), incision and drainage: 11 patients (14%), and scar revision: 12 patients (15%). All other reoperations occurred in less than 10% of patients. Type of additional surgical procedures data are summarized in Table 5.4.4.2-A for the three cohorts.

Among the 251 women in the Reconstruction cohort, 64 women (26%, 64/251) had 95 reoperation involving 82 implants, and 139 additional surgical procedures. By patient, the most frequently reported additional surgical procedures were: biopsy: 8 patients (13%) capsulectomy: 9 patients (14%), capsulotomy: 13 patients (20%), implant removal without replacement: 13 patients (20%), implant removal with replacement: 18 patients (28%), implant reposition: 12 patients (19%), and skin adjustment: 10 patients (16%).

Among the 205 women in the Revision cohort, 51 women 25% (51/205) had 100 reoperations involving 78 implants, and a total of 141 additional surgical procedures. The most frequently reported were biopsy: 7 patients (14%), capsulotomy: 11 patients (22%), capsulectomy: 12 patients (24%), implant removal without replacement: 11 patients (22%), implant removal with replacement: 14 patients (28%), scar revision: 6 patients (12%), and skin adjustment: 7 patients (14%).

Tables detailing reoperations and additional surgical procedures are included in Appendix D Tables 9.1 (type of additional surgical procedures), Table 9.2 (primary reason for

reoperation), Appendix D Table 9.3.1 (implant information), Appendix D Table 9.3.2 (reason for explant/reimplant with a study device), and Appendix D Table 9.3.3 (reason for implant removal). Appendix D Table 9.4 tabulates the primary reason for reoperation after explantation and reimplantation with a study device.

Table 5.4.4.2-A: Type of Additional Surgical Procedures by Patient at 3 Years, where Rate is Greater than 10%

Cohort	Complication	N	%
Augmentation N=79 patients	Capsulectomy	24	30
	Capsulotomy	12	15
	Implant removal without replacement	12	15
	Implant removal with replacement	15	19
	Incision and Drainage	11	14
	Scar Revision	12	15
Reconstruction N=64 patients	Biopsy	8	13
	Capsulectomy	9	14
	Capsulotomy	13	20
	Implant removal without replacement	13	20
	Implant removal with replacement	18	28
	Implant reposition	12	19
	Skin Adjustment	10	16
Revision N= 51 patients	Biopsy	7	14
	Capsulotomy	11	22
	Capsulectomy	12	24
	Implant removal without replacement	11	22
	Implant removal with replacement	14	28
	Scar revision	6	12
	Skin Adjustment	7	14

Table 5.4.4.2-B: Number of Reoperations and Additional Surgical Procedures by Indication at 3 Years

Indication	Number of			
	Reoperations	Additional Surgical Procedures	Patients	Implants
Augmentation	134	160	79	115
Reconstruction	95	139	64	82
Revision	100	141	51	78
Overall	329	440	194	275

5.4.5 Explantation Information through 3 Years

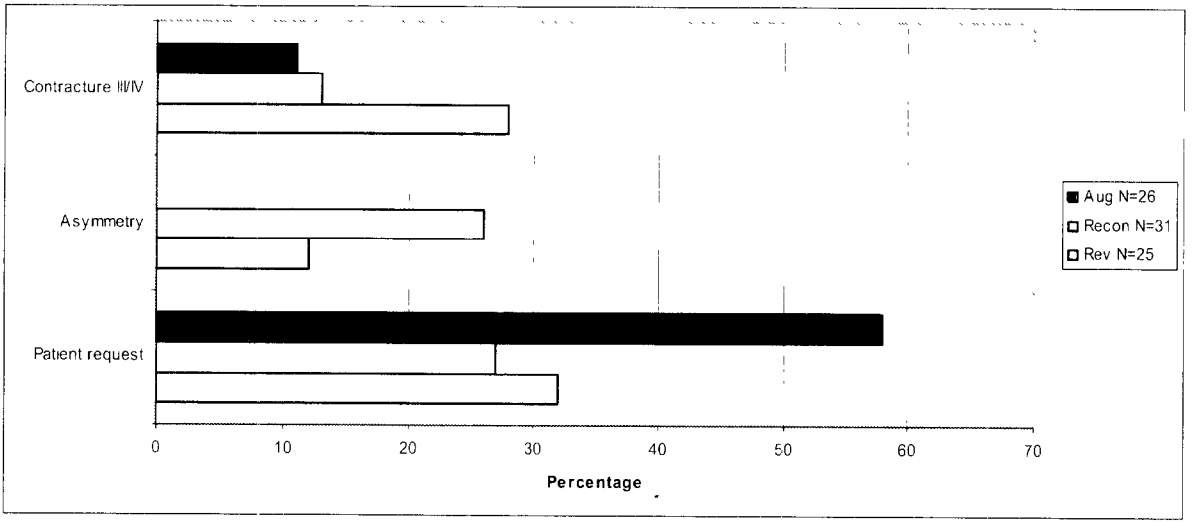
Among the 26 women in the in the Augmentation cohort who had explantations, the most frequently reported primary reasons were: patient request with 15 patients (58%, 15/26) and capsular contracture Baker Class III/IV with 5 patients (19%). All other reasons for explantation occurred in fewer than 10% of patients. Reason for explants are summarized in Figure 5.4.5-A below.

Among the 31 women in the Reconstruction cohort who had explantation, the most frequently reported primary reasons were: asymmetry with 9 patients (29%, 9/31), patient request: 8 patients (26%), and capsular contracture Baker Class III/IV: 4 patients (13%).

Among the 25 women in the Revision cohort who had explantation, the most frequently reported primary reasons were: patient request with 8 patients (32%, 8/25), capsular contracture Baker Class III/IV: 7 patients (28%), and asymmetry: 3 patients (12%).

Full details on explantations are provided in Appendix D Table 9.3.3.

Figure 5.4.5-A: Primary Reason for Explant by Patient at 2 years, where Rate is Greater than 10%



5.4.5.1 Kaplan-Meier Cumulative Incidence Rate of Complications after Explantation with Replacement by Study Device

Of the 82 patients explanted, 47 (57%) were reimplanted with a study device. Following reimplantation, 9 patients and 12 implants had at least one postoperative complication and 6 patients and 10 implants had at least one reoperation (does not include nipple tattoo and nipple reconstruction) by 3 years. Table 5.4.5.1-A below tabulates key complications reported following explantation with replacement using a study device. Complications after reimplantation are detailed in Appendix D Tables 8.18.1 and 8.18.2.

Table 5.4.5.1-A: Kaplan-Meier Cumulative Incidence Rates Through 3 Years Following Explantation with Replacement using a Study Device for Key Complications

Cohort	Complication	Patient		Implant	
		%	CI	%	CI
Augmentation N=15 patients	Capsular Contracture Grade III/IV	0	-	0	-
	Infection	0	-	0	-
	Rupture	0	-	0	-
	Any Reoperation	8.3	0,24	10.0	0,23.2
	Implant removal with replacement	0	-	0	-
	Implant removal without replacement	0	-	0	-
Reconstruction N=19 patients	Capsular Contracture Grade III/IV	6.5	0,18.0	5.0	0,14.6
	Infection	11.8	0,27.1	9.5	0,22.1
	Rupture	0	-	0	-
	Any Reoperation	12.6	0,19.0	15.3	0.31.4
	Implant removal with replacement	6.7	0.19.3	10.5	0,24.3
	Implant removal without replacement	0	-	0	-
Revision N=15 patients	Capsular Contracture Grade III/IV	18.0	0,40.9	12.6	0,29.1
	Infection	0	-	0	-
	Rupture	0	-	0	-
	Any Reoperation	297.	0.7,58.6	33.9	8.8,59
	Implant removal with replacement	0	-	0	-
	Implant removal without replacement	19.2	0,43.9	26.8	3.5, 50.1

5.4.6 Prevalence and Non-Cumulative Incidence of Complications

As specified by FDA's "Draft Guidance for Industry and FDA Staff – Saline, Silicone Gel, and Alternative Breast Implants," detailed tables on the prevalence and non-cumulative incidence of complications are provided in Appendix D Tables 22 and 23, as an alternative format for presentation of the complication data.

5.4.7 Cox Regression Analyses

Cox regression analyses were conducted to examine whether certain patient, device, and surgical characteristics are risk factors associated with clinical outcomes. In addition to variables specified in FDA's guidance document (age, race, smoking status, surgical approach, surgical placement, incision size, irrigation solutions used in the pocket, implant surface type) implant size, use of tissue expander, and investigator site were also evaluated. Of the 11 variables, 9 had significant effect on a complication in 1 or more of the cohorts. For example, prior use of a tissue expander was associated with a higher risk of infection in the Reconstruction cohort.

Significant Cox Regression findings are presented below in Table 5.4.7-A. For each variable, the reference is provided in the column entitled "Risk Factor Reference." Detailed results are presented in Appendix D Tables 10.1 through 10.10. For the Augmentation cohort, a subanalysis was performed where the submuscular and subpectoral categories were merged together. These analyses are presented as "A-suffixed" tables in Appendix D.

Table 5.4.7-A: Significant Cox Regression Findings

Complication	Cohort	Risk Factor	Risk Factor Reference	Significant Finding
Infection	Augmentation	Age	Age - continuous variable	Younger patients associated with higher risk
	Reconstruction	Tissue Expander	Pts with tissue expanders	Prior tissue expander associated with higher risk
Capsular Contracture Baker III or IV	Augmentation	Surgical Placement	Submuscular	Subglandular and Subpectoral at higher risk
	Reconstruction	Irrigation Solutions	Saline only	"Saline only" associated with higher risk "Antibiotic only" and "Other" associated with lower risk
	Revision	Investigator Site	Pooled sites	Three sites were associated with higher risk: 2, 10, and 19
Explantation With or Without Replacement	Augmentation	Surgical Approach	Inframammary	Transaxilliary and Other/Mixed associated with higher risk and Periareolar associated with lower risk
	Reconstruction	Race Age	Caucasians Age - continuous variable	"Other" associated with higher risk Younger patients associated with higher risk
Explantation without Replacement	Reconstruction	Race	Caucasians	"Other" associated with higher risk
Reoperation	Augmentation	Surgical Approach	Inframammary	Transaxilliary and Other/Mixed associated with higher risk and Periareolar associated with lower risk
	Reconstruction	Age Smoking Status Surgical Placement Implant Size	Age - continuous variable Nonsmokers Submuscular Implant Size – continuous variable	Older patients associated with higher risk Smokers associated with lower risk Subglandular and Other/Mixed associated with higher risk and Subpectoral associated with lower risk Larger implant associated with higher risk
Any Complication	Revision	Investigator Site	Pooled site	Three sites were associated with higher risk: 2, 10, and 19

* Where submuscular and subpectoral categories are merged

5.4.8 Deaths (All Due to Preexisting Breast Cancer)

Since the PMA submission in December of 2003, 2 additional patients had expired (estigators for these Reconstruction patients indicated that these deaths were all related to pre-existing breast cancer.

These events were promptly reported by the Investigators to both Mentor and the responsible IRB. There were no deaths reported in either the Augmentation or Revision cohorts.

5.4.9 Reproduction and Lactation - Preoperative History and Postoperative Experience

During the preoperative medical history, 214 of the 1,007 patients reported reproductive complications. A total of 718 (71%) patients reported live births prior to implant surgery. The number of miscarriages was not collected.

Postoperatively, through 3 years, 84 of the patients reported pregnancies. Nine patients reported a miscarriage.

Preoperatively, 496 patients reported that they had attempted to breastfeed, 492 patients reported no breastfeeding experience, and 19 patients did not answer the question. In regards to preoperative breastfeeding outcome, 467 patients reported that they had adequate milk, 94 patients reported inadequate milk, and the remainder chose not to respond. Postoperatively, 33 patients reported that they had attempted to breastfeed. Of these patients, 30 (91%) reported that they had adequate milk. Only 2 patients of the 33 (6%) had lactation difficulties. One of these patients was implanted via a periareolar incision, and the other via an inframammary incision.

Preoperative reproduction and lactation data are detailed in Appendix D Tables 4.1. Postoperative reproductive complications are tabulated along with other complications in Appendix D Tables 8.1 and 8.2.

5.4.10 Breast Cancer - Preoperative History and Postoperative Findings

In the Augmentation cohort, patients were excluded from the study if they had active cancer of any kind. Through 3 years postoperative, there were no occurrences of breast cancer in the Augmentation cohort.

Of the 251 Reconstruction patients, 169 had a history of breast cancer. Of these patients, 100 had been treated with chemotherapy; 35 had been treated with radiation; and 70 had been treated with hormonal therapy. Through 3 years postoperative, 1 patient (0.5%, 1/205) of the Revision cohort had a new diagnosis of breast cancer.

Breast cancer history and cancer treatment history for Reconstruction patients (includes Reconstruction and Reconstruction Revision cohort patients) are tabulated in Appendix D Table 6. The incidence of newly diagnosed breast cancer for all cohorts is tabulated along with other complications in Appendix D Tables 8.1 and 8.2.

5.4.11 Connective Tissue/Autoimmune/Rheumatic Disease - Preoperative History and Postoperative Complications

No patients reported a preoperative diagnosis of connective disease, autoimmune, or rheumatic disease, as this was an exclusion criterion for participation in the study. Six patients had a newly confirmed diagnosis of connective tissue, autoimmune, or rheumatic disease during the 36-month follow-up period (3 Augmentation, 1 Reconstruction, and 2 Revision patients). These diagnoses included 1 of Hashimoto Thyroiditis, 2 fibromyalgia, 1 pyoderma gangrenosum, 1 rheumatoid arthritis, and 1 hypothyroidism. Details on these six patients, including implant type, placement, time to onset, rupture status, and adverse events is included in Table 5.4.11-A.

Rheumatic symptoms and diseases are fully detailed in Appendix D Table 11.1 through 11.4. The estimated cumulative incidences based upon Kaplan-Meier Cumulative Incidence estimates for any newly developed rheumatic disease, for specific rheumatic disease diagnoses, for symptoms by system category, for symptom type, and for physical examination findings are presented in Appendix D Tables 8.7.1, 11.5, 11.6, 11.7, and 11.8 respectively.

5.4.11-A: Information on Patients with New Diagnosis of Connective Tissue/Autoimmune/Rheumatic Disease

Pt. ID	Patient Information	Diagnosis	Time to Onset of Diagnosis	Rupture Status	Summary	Adverse Events
	Cohort: Augmentation **DOS:** **Implant Type:** textured round gel **Placement:** subglandular **MRI Substudy:** YES **MRI Scan Dates:** 1/11/02 11/22/02 **Investigator**	Hashimoto's Thyroiditis	17 months (date reported: April 2002)	No rupture	Hashimoto's thyroiditis diagnosed at 2 year visit. Documented with rheumatology consult.	New diagnosis of rheumatic disease 4/2002 Right unacceptably low nipple sensitivity 11/8/00
	Cohort: Augmentation **DOS:** **Implant Type:** smooth round gel **Placement:** subglandular **MRI Substudy:** NO **MRI Scan Dates:** 8/29/ **Investigator**	Rheumatoid arthritis	19 months (date reported: May 2003)	No rupture	At her two year visit, this patient reported multiple symptoms and she was referred to a rheumatologist. Doctor's notes state the patient says she probably had symptoms prior to surgery, although she did not report any at her baseline visit. Reported seronegative rheumatoid arthritis at 2 year visit.	New diagnosis of rheumatic disease 5/2003 Bilateral Baker III capsular contracture 7/2002
	Cohort: Augmentation **DOS:** **Implant Type:** smooth round gel **Placement:** subpectoral **MRI Substudy:** NO **MRI Scan Dates:** n/a **Investigator**	Hypothyroidism	32 months (date reported: June 2002)	Not scanned	At the two year visit, this patient reported multiple symptoms and she was referred to a rheumatologist. Rheumatoid arthritis reported at 2 year visit. Arthritis not mentioned in 2-year rheumatology consult. Consult was reviewed by a rheumatology expert who indicated patient had hypothyroidism and as a result has thyroiditis, which is autoimmune in origin.	New diagnosis of rheumatic disease 6/2002
	Cohort: Revision **DOS** **Implant** ...ured round gel **Placement:** submuscular **MRI Substudy:** YES **MRI Scan Dates:** 8/26/03 **Investigator**	Fibromyalgia	12 months (date reported 2002)	No rupture	At her two year visit, this patient reported multiple symptoms and she was referred to a rheumatologist who confirmed diagnosis of fibromyalgia	New diagnosis of rheumatic disease 9/2002

New Diagnoses of Connective Tissue, Rheumatoid, and Autoimmune Disease

Pt ID	Patient Information	Diagnosis	Time to Onset of Diagnosis	Rupture status	Summary	Adverse Events
	Cohort: Augmentation **DOS** **Implant Type:** textured round gel **Placement:** subglandular **MRI Substudy:** YES **MRI Scan Dates:** **Investigator**	Hashimoto's Thyroiditis	17 months (date reported April 2002)	No rupture	Hashimoto's thyroiditis diagnosed at 2 year visit. Documented with rheumatology consult	new diagnosis of rheumatic disease R- unac low nipple sensit
	Cohort: Augmentation **DOS:** **Implant Type:** smooth round gel **Placement:** subglandular **MRI Substudy:** NO **MRI Scan Dates** **Investigator:**	Rheumatoid arthritis	19 months (date reported. May 2003)	No rupture	At her two year visit, this patient reported multiple symptoms and she was referred to a rheumatologist Doctor's notes state the patient says she probably had symptoms prior to surgery, although she did not report any at her baseline visit Reported seronegative rheumatoid arthritis at 2 year visit	New diagnosis of rheumatic disease 5/2003 Bilateral Baker III capsular contr
	Cohort: Augmentation **Implant Type:** smooth round gel **Placement:** subpectoral **MRI Substudy:** NO **MRI Scan Dates:** n/a **Investigator:** (#41,	Hypothyroidism	32 months (date reported. June 2002)	Not scanned	At the two year visit, this patient reported multiple symptoms and she was referred to a rheumatologist Rheumatoid arthritis reported at 2 year visit. Arthritis not mentioned in 2-year rheumatology consult. Consult was reviewed by a rheumatology expert who indicated patient had hypothyroidism and as a result has thyroiditis, which is autoimmune in origin.	New diagnosis of rheumatic disea
	Cohort: Revision **DOS** **Implant Type:** textured round gel **Placement:** submuscular **MRI Substudy:** YES **MRI Scan Dates:** **Investigator.**	Fibromyalgia	12 months (date reported 2002)	No rupture	At her two year visit, this patient reported multiple symptoms and she was referred to a rheumatologist who confirmed diagnosis of fibromyalgia	New diagnosis of rheumatic

Pt. ID	Patient Information	Diagnosis	Time to Onset of Diagnosis	Rupture Status	Summary	Adverse Events
	Cohort: Revision **DOS:** **Impla** mooth round gel **Placement:** submuscular **MRI Substudy:** NO **MRI Scan Dates:** n/a **Investigator**	Pyoderma gangrenosum	12 months (date reported: June 2002)	No scan	Pyoderma gangrenosum diagnosed at 1 year. Dermatologist treating her with steroids for pyoderma gangrenosum. A rheumatology expert reviewed the documents and said this patient could have an autoimmune disease, and it is usually associated with IBS or Crohn's disease. To be conservative, it is being reported as a new diagnosis of rheumatic disease.	New diagnosis of rheumatic disease 2/2002 Left breast pain not associated with other complication 8/9/01 Infection 7/30/01
	Cohort: Reconstruction **DOS:** 11/13/01 **Implant Type:** textured round gel **Placement:** submuscular **MRI Substudy:** YES **MRI Scan Dates:** 7/25/02, 8/26/03 **Investigator:** ile	Fibromyalgia	9 months (date reported: July 2002)	No rupture	At the 1 year visit, patient reported multiple symptoms and was referred to a rheumatologist who confirmed diagnosis of fibromyalgia.	Asymmetry on Right side 1/28/02

5.4.12 Mammography

Mammograms were not required as part of this study. Additionally, the average age of the study patients is below the age at which mammograms are typically recommended. Nevertheless, approximately 25% of the patients underwent postoperative mammograms. Through 3 years, 11 (4.1%) patients had a postoperative mammographic report of an abnormal mass (6, 1, and 4 among Augmentation, Reconstruction, and Revision patient cohorts, respectively).

Appendix D Table 12.1 presents the results for breast mammogram assessments at follow-up visits, relative to preoperative mammogram results. The incidence of newly diagnosed breast cancer is tabulated along with other complications in Appendix D Tables 8.1 (patient level) and 8.2 (implant level). The incidence of new postoperative abnormal mammogram results is tabulated regardless of biopsy results in Appendix D Table 12.2.1 (patient level) and Table Appendix D 12.2.2 (implant level), and by biopsy result in Appendix D Table 12.2.3 (implant level). The estimated Kaplan-Meier Cumulative Incidence rates based on Kaplan-Meier estimates are presented in Appendix D Tables 8.7.1, 12.3.1 (patient level regardless of biopsy), Appendix D Tables 8.7.2, 12.3.2 (implant level regardless of biopsy), and Appendix D 12.3.3 (implant level by biopsy result).

5.4.13 Rupture and Extracapsular Silicone Gel

The rupture rate analysis was conducted using only patients participating in the MRI substudy. This population of patients was used as the basis for estimating the overall rupture rate, as it is only in this sample that both silent ruptures and overt ruptures would have been detected.

As discussed in the FDA-approved Core Gel protocol, 320 patients would be adequate to detect a silent rupture of 5%. To account for lost to follow up, 405 patients were to be enrolled, but Mentor actually enrolled 420 patients into the MRI substudy. As summarized in Table 5.4.13-A below, 89% (372 patients) had returned for their 2-year scan, at the time of database lock. The number of actual patients in the MRI Substudy and the high follow up rate demonstrate that this patient population is adequate to determine the rupture rate for the Mentor Silicone Gel-Filled Breast Implants.

Table 5.4.13-A: MRI Substudy Patient Accounting for 2-year MRI Scan

Category	Augmentation	Reconstruction	Revision	Overall
Theoretically due[1]	202	134	84	420
Deaths	0	1	0	1
Patients with all devices removed without replacement	0	1	0	1
Patients with all devices removed and replaced with other manufacturer's devices[2]	0	0	0	0
Patients with all devices removed and replaced with Mentor Core Gel devices[2]	0	0	0	0
Patients not yet due for follow up[3]	0	0	0	0
Expected[4]	202	132	84	418
Actual (Patients with complete follow-up)	182	117	73	372
Percent Follow-up (Actual/Expected)	91%	89	87	89

1 Patients who would have been examined according to implant date and follow-up schedules.
2 Data not collected
3 Patients who have not yet had the 2nd anniversary of their surgery.
4 Patients theoretically due minus deaths minus removals without replacement and removals with replacement with different manufacturer's devices minus patients not yet due for follow up

The following hierarchy (in descending order) was used to determine whether or not a rupture (including "silent" ruptures) occurred. Specifically, the first available of these listed determinations was used. Determination based on visual examination of the device by Mentor was used whenever available.

1. Determination based on visual examination by Mentor following explantation of the implant.
2. Determination based on physical examination by surgeon following explantation of the implant, as indicated on Adverse Event Case Report Form. Implementation of this aspect of the hierarchy was predicated on the assumption that, upon examination of an explanted device, the surgeon would, if needed, update the AE CRF. Specifically, (1) if a rupture was newly identified upon examination, the rupture would be recorded and (2) if an implant which had been previously recorded as ruptured was determined, upon examination, to be intact, the previously recorded rupture would be deleted.
3. Determination based on MRI findings without explantation of the implant, as indicated on Adverse Event Case Report Form. MRI finding was given precedence over the surgeon's finding (4 below) without explantation, unless the surgeon has a finding of rupture in a year subsequent to the (last) MRI. A device was considered to be ruptured if either the local radiologist or the Central MRI reviewer indicated any of the following:
   - evidence of rupture;
   - evidence of extracapsular silicone;
   - indeterminate for rupture; or
   - indeterminate for extracapsular silicone.

   If a follow up MRI was read by both the local radiologist and the Central Reviewer as not being ruptured, the implant was then considered not to be ruptured.
4. Determination based on surgeon's findings without explanation of the implant, as indicated on Adverse Event Case Report Form. MRI finding (3 above) was given precedence over the surgeon's finding without explantation unless the surgeon has a finding of rupture in a year subsequent to the (last) MRI.

5.4.13.1 Rupture Rate

As defined in Section 5.1.13 above, the overall cumulative incidence of rupture for Mentor's Silicone Gel-Filled Breast Implants was 0.7% and 0.5% for patients and implants, respectively (see Table 5.4.13-A).

5.4.13.1-A: Core Gel Cumulative Rupture Rates by Patient and Implant

Indication	Patient	Implant
Aug	0.2	0.1
Recon	0.6	0.4
Rev	2.5	2.0
Overall	0.7	0.5

There were 2 implants that were confirmed as ruptured upon explant. This gives a confirmed rupture rate of 0.2% by patient and 0.3% by implant. In addition, there were 6 suspected ruptures. Hence there are a total of 8 devices (6 patients) with ruptures as defined in 5.4.13. This is summarized by cohort in Table 5.4.13.1-B below. Table 5.4.13.1-C provides a history for each patient for who rupture was suspected and/or confirmed.

Table 5.4.13.1-B: Number of Device Considered to be Ruptured

Subject	Indication	Patients	Implants
	Revision	1	2
	Augmentation	1	1
	Revision	1	2
	Revision	1	1
	Reconstruction	1	1
	Revision	1	1
	Total	6	8

The number of patients and implants in the MRI substudy is tabulated overall and by indication in Appendix D Table 13.1. MRI Substudy patient accounting is Appendix D Table 13.3. Cumulative incidence of rupture is detailed in Appendix D Table 8.7.1.

5.4.13.2 Non-MRI Substudy Rupture Findings

There have been no confirmed ruptures in patients outside the MRI Substudy cohort.

Through 3 years, there was 1 patient not participating in the MRI substudy, for whom possible rupture was reported. Patient 435.014 was a Revision patient, who had her non-Core Study ruptured implants removed, prior to being implanted with Core devices. Subsequently, she had a routine mammogram, and it was noted to have extracapsular silicone in the left breast, when read by the local radiologist,. A follow up MRI read by the local radiologist indicated possible extracapsular silicone and rupture of the left breast implant. Mentor's Central Reviewer reviewed the scan and said the implant was intact, but noted a mass. The patient elected to have the implant removed, at which time the doctor noted the implant was intact. Mentor's Product Evaluation Department confirmed that the device was intact. Based on intact Core Gel implants being removed, it is presumed that the extracapsular gel noted was from this patient's previously ruptured non-Core Gel implants.

History for each Patient for who Rupture was Suspected and/or Confirmed

Pt. ID	Patient Information	History (Hx)	Local Reader	Central Reviewer	Final Determination of Rupture Status	Method of Determination	Adverse Events
	Cohort: Revision **DOS:** **Implant Type:** textured round gel **Placement:** subglandular M M	Prev ruptured right implant, MRI reported Ruptures	Bilateral ruptures	Bilateral Ruptures	Bilateral Ruptures	Explanted. Ruptures confirmed by Product Evaluation. Patient had implants replaced.	Bilateral ruptures onset date unknown Concomittant surgeries: Catherization and thrombectomy L hand for blood clots 10/1/01, Amputation L hand lood clots
	Cohort: Augmentation **DOS:** **Implar** oth round gel **Placement:** subglandular **MRI Substudy:** YES **MRI Scan Dates:**	Possible rupture on right per local MRI reader	possible rupture on right	No rupture	No rupture	No physical findings of rupture Plastic surgeon felt area of concern was buckle in the implant.	Wrinkling
	Cohc sion **DOS:** **Implant Type:** textured round gel **Placement:** subpectoral **MRI Substudy:** YES **MRI Scan Dates:** **Investigator.**	Previously ruptured implants & silicone granulomas ossible xtracapsular silicone on right per MRI	indeterminate for extracapsular rupture on right, correlate with hx of previous implants, current implants intact	Indeterminate for extracapsular rupture on right, correlate with hx of previous implants, current implants intact	No rupture, indeterminate for extracapsular silicone Hx of ruptured gel implant in 1985	Patient had ultrasound 5/12/04. No rupture. No mention of extracapsular silicone in the report Radiologist recommended repeat MRI	R breast trauma sustained in car accident 2/12/02. Note. no adverse event submitted as occurrence was not device or procedure related.
	Cohort: Revision oth round gel **Placement:** subglandular **MRI Substudy:** YES **MRI Scan Dates:** **Investigator:**	Post closed capsulotomy, possible rupture on the left per local MRI reader	rupture on left side	No rupture	No rupture	Mentor recommended repeat scan Patient has yet to return for re-scan	L - Hematoma 4/24/01 R - Nipple Unacceptably Low Sensitivity 4/18/01 L - Nipple Unacceptably Low Sensitivity 4/18 01 L - Baker III Capsular Contracture 1 17/02 L - Breast Unacceptably Low Sensitivity 2/24/03

5.5 Effectiveness

Implantation of Mentor Gel-Filled Breast Implants resulted in significant increase in circumferential chest size and bra cup size in the Augmentation cohort and restoration of the chest mound in the Reconstruction and Revision cohorts.

5.5.1 Primary Effectiveness Endpoint – Circumferential Chest Size and Bra Cup Size

The primary effectiveness endpoint was assessed based primarily on changes in chest circumference and bra cup size (Augmentation cohort only).

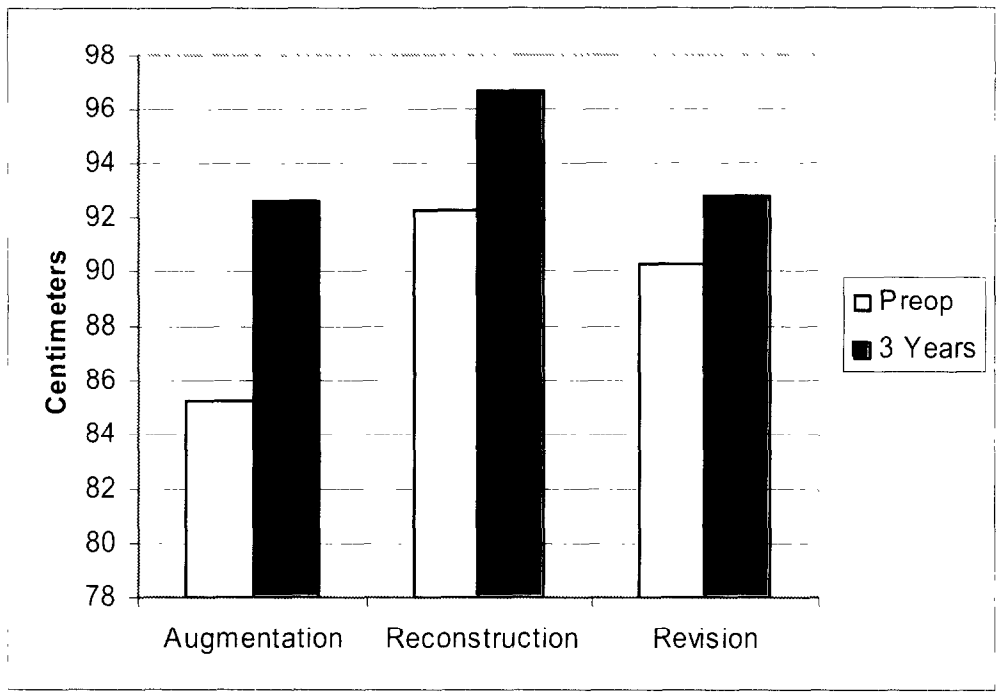
5.5.1.1 Circumferential Chest Size

For patients overall and for all three indications, the changes over the course of the study in circumferential chest size were positive and highly significant. The overall mean change from baseline measurements was greatest among Augmentation patients (7.1 cm). Table 5.5.1.1-A below summarizes the overall mean changes in circumferential chest size (measured at the level of the nipple) over the course of the study. Figure 5.5.1.1-A below details the mean chest size in centimeters for each of the three cohorts. Circumferential chest size is fully detailed in Appendix D Tables 14.1 and 14.2.

Table 5.5.1.1-A: Change in Mean Circumferential Through 3-Year

Cohort	Baseline (centimeters)	Overall Mean Change (centimeters)	p-value
Overall	87.8	5.4	<0.0001
Augmentation	85.2	7.1	<0.0001
Reconstruction	92.3	3.3	<0.0001
Revision	90.3	2.8	<0.0001

Figure 5.5.1.1-A: Mean Circumferential Chest Size at Baseline and 3-years



5.5.1.2 Bra-Cup Size for Augmentation Cohort

For the Augmentation cohort, the average bra cup increase from baseline across all follow-up visits was 1.7 cup sizes and was statistically significant (p-value <0.0001). This is summarized below in Table 5.5.1.2-A. Bra-cup size assessment is detailed in Appendix D Tables 15.1 and 15.2

Table 5.5.1.2-A - Bra Cup Size Change from Preoperative to 3 Years Postoperative for the Augmentation Cohort. N=370

Cohort	No Change		1 Cup		2 Cups		3 Cups		≥ 4 Cups	
	n	%	n	%	N	%	n	%	n	%
Augmentation*	11	3.0	126	34.1	185	50.0	48	13.0	0	0.0

* 27 patients did not have Bra Cup size measured at 3 years

5.5.2 Secondary Effectiveness Endpoint - Quality of Life

5.5.2.1 Global Patient Satisfaction

At the 3-year follow-up visit, overall 97% of patients indicated they would have the surgery again. The results were similar for all 3 cohorts: 97%, 98%, and 96% for Augmentation, Reconstruction, and Revision respectively. Furthermore, 93% of reoperation patients indicated that they would have the surgery again. Global Satisfaction is detailed in Appendix D Table 21.

5.5.2.2 Tennessee Self-concept Scale

The Tennessee Self-concept Scale is intended to summarize an individual's feeling of self-worth, the degree to which the self-image is realistic, and whether or not that self-image is a deviant one.

Among the Augmentation and Reconstruction cohorts there was no significant change in the overall mean value of the total score across follow-up visits. Among Revision patients there was a statistically significant decrease of 6.6 in the overall mean value of the total score across follow-up visits, suggesting a decline in self-concept as measured by this assessment.

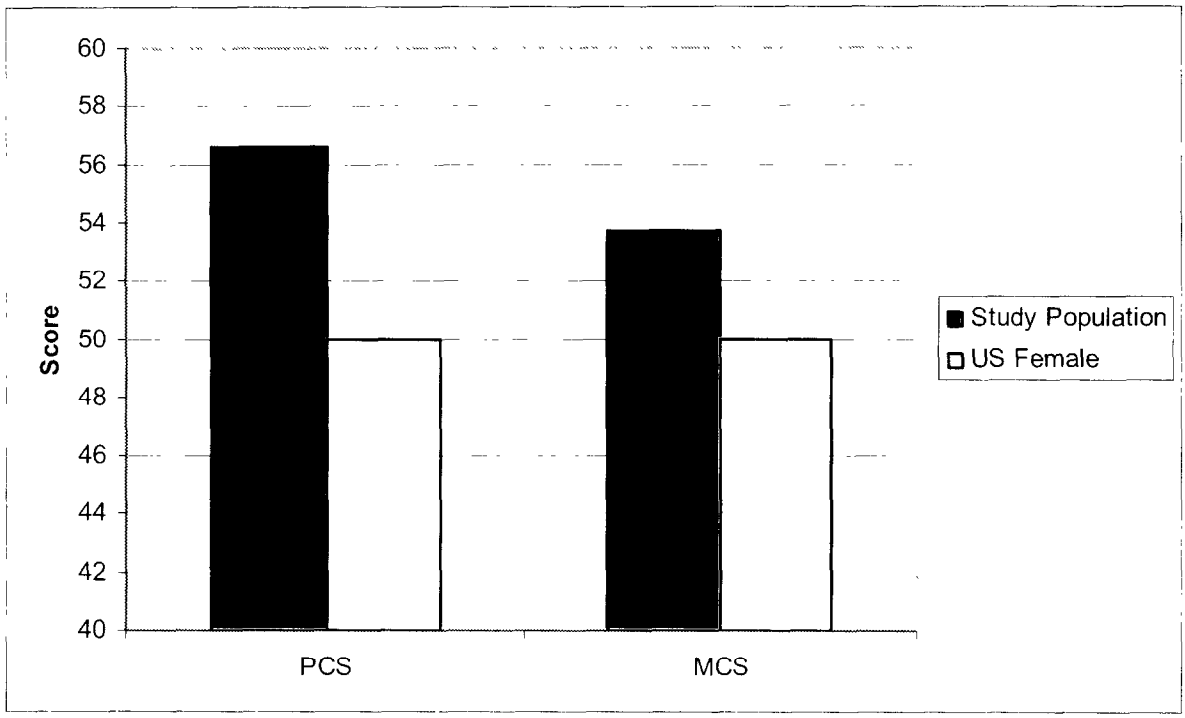
The total score was analyzed by device placement. For submuscular placement, a statistically significant overall mean increase (3.4) was observed for Augmentation patients, no significant difference reported for Reconstruction patients, and a statistically significant overall mean decrease (8.0) was observed for Revision patients. Appendix D Table 16.1 summarizes results for the total score, while Table 16.2 repeats the analysis by device placement.

5.5.2.3 Short Form 36 (SF-36)

The SF-36 yields an 8-scale profile of functional health and well-being scores as well as psychometrically based summary measures – the Physical Component Score (PCS) and Mental Component Score (MCS). It is a generic measure, as opposed to one that targets a specific age, disease, or treatment group.

At baseline, the overall patient population scored significantly higher than the general United States female population on all 8 subcategories. As shown in Table 5.5.2.3-A the study population also scored significantly higher then the US female population on the Mental Component Score (MCS) and Physical Component Score (PCS).

Table 5.5.2.3-A: SF-36 MCS and PCS Comparison of Study Population to US Female Population



The results for some of the subscales showed scores that decreased slightly from preoperative to postoperative assessment. However the magnitude of these changes was slight. Postoperatively, the study populations continued to score higher for all eight subcategories and the MCS and PCS, as compared to the US female population.

Appendix D Tables 17.1 and 17.2 detail results for the Physical Component Summary Scale and the Mental Component Summary Scale, respectively. Appendix D Tables 17.3 and 17.4 repeat these analyses by device placement.

5.5.2.4 Body Esteem Scale (BES)

The BES measures female body esteem. For women, assessments include sexual attractiveness, weight concern, and physical condition.

Among the Augmentation and Reconstruction cohorts there was no significant change in the overall mean value of the total score across follow-up visits. Among Revision patients there was a statistically significant decrease of 5.0 in the overall mean value of the total score across follow-up visits, indicating a lowering of their overall level of body-esteem, as measured by the Body Esteem Scale.

However, revision patients represent a uniquely difficult population from a medical and psychological perspective, therefore greater difficulties, while unfortunate, are not unexpected.

The total score of the Body Esteem Scale is detailed in Appendix D Table 18.1 and stratified by device placement in Appendix D Table 18.2.

5.5.2.5 Rosenberg Self-esteem Scale

The Rosenberg SES is used to assess global and unidimensional self-esteem, relating to an individuals overall feelings of self-worth or self-acceptance.

Among the Augmentation patients there was a statistically significant positive change of 0.6 in the overall mean value of the total score across follow-up visits. This indicates an increase in self-esteem based upon this instrument. There were no changes among the Reconstruction and Revision patients.

When the results are stratified by device placement, within Augmentation patients statistically significant increases were noted for patients having a device implanted using a submuscular approach (mean increase of 0.8) or a subpectoral approach (mean increase of 0.7). There were no changes among the Reconstruction and Revision patients.

The total score of the Rosenberg Self-esteem Scale is detailed in Appendix D Table 19.1 regardless of device placement and in Appendix D Table 19.2 stratified by device placement.

5.5.2.6 Functional Living Index: Cancer (FLIC)

The FLIC is a subjective instrument designed to assess physical well-being, psychologic state, family situational interaction, social ability, and somatic sensation

A statistically significant overall mean increase in the FLIC score was noted for delayed post-mastectomy patients (mean increase of 2.9), indicating improved functioning from pre- to postoperative. A statistically significant overall mean increase was also noted among revision patients who had a least one reconstruction revision or revision of an unknown indication, and a history of cancer (mean change of 5.0). Device placement did not affect the results of these tests.

The total score of the FLIC is detailed in Appendix D Table 20.1 and in Appendix D Table 20.2 stratified by device placement.

6.0 DISCUSSION AND CONCLUSIONS

The results of the Core Gel Study of Mentor's Silicone Gel-Filled Breast Implants demonstrate that these devices are safe and effective for their intended uses for aesthetic augmentation of the female breast for cosmetic purposes, reconstruction of the female breast following mastectomy or other conditions that result in deformities of the breast, and revision of pre-existing implants. Mentor requests that FDA approve these devices for commercial distribution in the US.

The study was designed as a 10-year prospective clinical study in accordance with the Food and Drug Administration's then current "Guidance for Saline, Silicone Gel, and Alternative Breast Implants: Final Guidance for Industry and FDA," and in consultation with experts from a variety of medical disciplines. Mentor is submitting this PMA update with patient follow-up data through 3 years post-implantation. Patients will continue to be followed by their physicians at 4, 5, 6, 7, 8, 9, and 10 years post surgery. There were 1,007 female patients (551 Augmentation, 251 Reconstruction, and 205 Revision patients) enrolled by 40 Investigators in the Core Study. At three years, the follow-up rate was 94% for the Augmentation cohort, 95% for the Reconstruction cohort, and 93% for the Revision cohort. These follow-up rates exceed the 80% goal outlined in the FDA Guidance and provide an adequate number of patients for statistical analysis.

The characteristics of the patients enrolled in the Core study can be summarized as follows: 63% of the women were between the ages of 30 to 49, over 60% were married at the time of implant surgery, more than 80% had some college experience, and 90% were Caucasian. The overall baseline demographics of the women who participated in this study are comparable to the profile of women who participated in Mentor's Saline Prospective Study (SPS)[8] and to the US population of women undergoing augmentation and reconstruction procedures with mammary prostheses,[9] providing confidence in the relevance of these findings to the larger population of potential augmentation, reconstruction, and revision patients.

With regard to safety, patients enrolled in the Mentor Core Gel study exhibited 3-year complication rates similar to or lower than those previously reported for breast implants. For the overall study population, the Kaplan-Meier Cumulative Incidence rates for key complications were: capsular contracture 9.2%, infection 2.3%, rupture 0.8%, any reoperation 20.2%, and explantation with or without replacement 8.8%.

Most patients experienced a resolution to their reported complications by their 3-year follow-up visit. In the overall patient population, more than 33% of the reported complications resolved without any type of treatment. Patients whose complications have not resolved within 3 years are either undergoing treatment, had previously refused treatment, or had a complication for which treatment was not possible (e.g., unacceptably low breast sensitivity in the Reconstruction cohort). For those complications that required treatment, over 97% were resolved without the need for hospitalization. Of those patients whose devices were explanted, 57% chose to be reimplanted.

The cumulative incidence rates by patient for several key complications (rupture, capsular contracture, infection, reoperation, and implant removal/replacement) in the Mentor Core Gel clinical trial are described below by cohort, followed by a comparison of these rates to those reported in clinical trials for other breast implants, and the published literature (see Table 6.0-A and 6.0-B below).

Through 3 years, there have been two confirmed device ruptures and six suspected ruptures, a rupture rate of 0.8%. This rupture rate is lower than the 1 to 2% rupture rate reported in the 10th year Mentor Adjunct Breast Implant Annual Report,[10] as well as the rupture rates reported for Inamed's silicone gel-filled implants, Mentor's saline implants (deflation), and the published literature, as shown in Table 6.0-A below.

Capsular contracture was reported in 8.2% of patients in the Augmentation cohort, 8.8% of patients in the Reconstruction cohort, and 17.2% of patients in the Revision cohort. Infection was reported in 1.5% of patients in the Augmentation cohort, 5.3% of patients in the Reconstruction cohort, and 1.0% of patients in the Revision cohort. Reoperations were performed in 15.0% of patients in the Augmentation cohort, 26.3% of patients in the Reconstruction cohort, and 26.3% of patients in the Revision cohort. Some of the most common types of reoperations across cohorts were: capsulectomy, open capsulotomy, implant reposition, scar revision, skin adjustment, and incision and drainage. The rate of reoperations in the Reconstruction cohort is higher than that observed in the Augmentation cohort, consistent with literature. The reconstruction process typically involves multiple procedures to achieve the intended aesthetic result, including multiple and staged procedures to obtain symmetry. The higher rate observed among the revision patients is also consistent with clinical experience reported in the literature. Implants were removed with or without replacement in 5.1% of the Augmentation cohort, 13.3% of the Reconstruction cohort, and 13.2% of the Revision cohort

The cumulative risk rates for complications reported in the Mentor Core Gel study are generally comparable to or lower than those observed in similar clinical studies of Mentor and Inamed gel breast implants, consistent with the published literature. The 3-year Kaplan-Meier cumulative complication rates observed in these studies and the literature are provided in Tables 6.0-A and 6.0-B below. Importantly, the cumulative risk rates for ruptures and explants were lower for Mentor's gel implants than Mentor's saline implants for both augmentation and reconstruction patients; the cumulative risk rates for rupture and reoperations were lower for Mentor's gel implants than Inamed's gel implants for both augmentation and reconstruction patients, and the implant removal with and without replacement cumulative risk rates for Mentor's gel implants were lower than Inamed's gel implants in reconstruction patients.

The cumulative risk rates for infection and capsular contracture in the Mentor Core Gel study are within the rates reported in the literature. The infection rates were somewhat higher than in the Inamed gel study for the Augmentation, Reconstruction, and Revision cohorts. The infection rates were similar or lower to the corresponding risk rates observed in Mentor's Saline Prospective Breast Study (SPS) study. Moreover, infection is surgically-related, rather than a device-specific complication. The capsular contracture rates were similar to or lower than those reported in Inamed's gel study for the Reconstruction cohort, but were higher in the Reconstruction and Revision cohorts. The Core Gel capsular contracture rates was slighter higher in the Augmentation cohort and markedly lower in the Reconstruction cohort than the corresponding risk rates observed in Mentor's SPS study.

The results of Mentor's Core Gel study provide evidence that Mentor's Silicone Gel-Filled Breast Implants do not adversely affect pregnancy or lactation outcomes. Through 3-years postoperative, 62 of the patients reported pregnancies. Of those, 9 patients (15%) reported miscarriages. This rate is comparable to the 15.7% miscarriage rate reported for the general US population,[11] indicating that in this study, the Mentor Silicone Gel-Filled Breast Implants did not have an affect on the rate of miscarriage.

Postoperatively, 33 patients reported that they had attempted to breastfeed. Of these patients, 30 (91%) reported that they had adequate milk. Only 2 patients (6%) had lactation difficulties, and these patients were implanted via either a periareolar incision or an inframammary incision. These rates appear similar to the general US population.[12] Based on these Core Study results, Mentor Silicone Gel-Filled Breast Implants do not appear to increase the likelihood of experiencing lactation problems after implantation.

At the time of this update, 9 study patients have died. All were the result of preexisting breast cancer in the Reconstruction cohort. There were no deaths reported in either the Augmentation or Revision cohorts, and no suicides were observed in this study.

Cox regression analyses were conducted to examine whether certain patient, device, and surgical characteristics are possible risk factors associated with clinical outcomes. These analyses frequently can lead to valuable clinical conclusions concerning, for example, patient selection and surgical technique. The results of Cox regression analyses also may suggest factors warranting further investigation to determine their clinical significance.

Cox regression analyses findings from the present study that suggest valuable clinical information, include the following potential relationships: younger patients, inframammary approach, submuscular placement, smaller implant size, and use of irrigation solutions containing antibiotics generally reduce the risk of Baker Grade III or IV capsular contracture and/or reoperation.

The association between silicone gel-filled breast implants and the occurrence of breast cancer has been the subject of much debate over the last several decades. In the present study, at the end of the 3-year postoperative period, no occurrences of breast cancer were reported in the Augmentation and Reconstruction cohorts, and only one new occurrence of breast cancer was reported in the Revision (0.5%) cohort. This rate of occurrence falls within the incidence rate reported in the US population (0.0014%-0.5% for women aged 20-79 years[13]), indicating that, in this study, Mentor's Silicone.Gel-filled breast implants are not associated with an increased incidence of breast cancer. This finding is consistent with the lack of association between silicone breast implants and cancer demonstrated in numerous epidemiological studies.

The association between silicone gel-filled breast implants and connective tissue/rheumatic disease is also the subject of debate. In the present study, patients were excluded from being implanted with a Core device, if they had a preoperative confirmed diagnosis of a rheumatic disease.

Six patients had a new diagnosis of rheumatic disease during the 3-year follow-up period (1 of Hashimoto Thyroiditis (0.1%), 2 fibromyalgia (0.2%), 1 pyoderma gangrenosum (0.1%), 1 rheumatoid arthritis (0.1%), and 1 hypothyroidism (0.1%)). The observed incidence rate of these diseases in the Core Study was below that of the general US population (the estimated incidence of thyroiditis (including Hashimoto and other) and rheumatoid arthritis is reported to be 0.8% and 0.9%, respectively,[14] the incidence of fibromyalgia is reported to be 3.4%,[15] and the incidence of pyoderma ganjgrenosum is reported to be 0.6% (in patients with ileostomy and inflammatory bowel disease[16]). The findings in the present study are consistent with the lack of association between silicone breast implants and connective tissue and rheumatic diseases demonstrated in numerous epidemiological studies.

While mammograms were not required as part of the Core Gel study, and the average age of the study patients is below the age at which mammograms are typically recommended, 25% of the patients had a postoperative mammogram.

In terms of the primary effectiveness endpoint, Mentor's implants were demonstrated to be highly effective in increasing the size of a woman's breast. These devices produced a significant increase in circumferential chest size and bra cup size in the Augmentation cohort, and a significant increase in circumferential chest size in the Reconstruction and Revision cohorts.

Several Quality of Life (QoL) instruments were used as secondary measures of effectiveness, to assess general health-related concepts, self concept, self-esteem, and body esteem. The QoL instruments included the Tennessee Self-concept Scale, the SF-36 Health Survey, Body Esteem Scale, the Rosenberg Self-esteem scale, and Treatment & Research Foundation Functional Living Index. For the majority of general health concepts, average scores at 3 years post-implant showed a statistically significantly decrease versus baseline. However the magnitude of the differences was small and the Quality of Life scores remained well above those of the general US female population.

The small decreases that were observed in some of the Quality of Life scales utilized in this study may be related to the very high scores that were observed among patients at baseline. Compared to the general US female population, the patients who enrolled in this study had significantly higher QoL scores, both pre and post implant.

Some of the scores decreased slightly, but statistically significantly, from preoperative to postoperative assessment. The study populations generally scored higher as compared to the general US female population. For example, for the SF-36, the study population scored significantly higher preoperatively and postoperatively, as compared to the US female population. Additionally, when a group with very high initial scores demonstrates a decrease in scores upon retesting, a common statistical phenomenon referred to "regression to the mean," is said to occur.[17]

Importantly, when patients were asked if they would have the surgery again, 97% of all patients indicated they would. Furthermore, for those patients who had reoperations, 93% indicated they would have the surgery again.

In conclusion, the results of this study demonstrated that Mentor Silicone Gel Breast Implants are safe and effective for their intended uses for aesthetic augmentation of the female breast for cosmetic purposes, reconstruction of the female breast following mastectomy or other conditions that result in deformities of the breast, and revision of pre-existing implants. The results presented in this report demonstrate that the cumulative risk rates for complications reported in the Mentor Core Gel study are generally comparable to or lower than those observed in similar clinical studies of Mentor and Inamed gel breast implants and consistent with the published literature. Moreover, the overwhelming majority of women who undergo breast implant surgery with Mentor Silicone Gel-Filled Breast Implants would have the surgery again, indicating a high level of satisfaction.

Table 6.0-A: Comparison Mentor Core Complication Rates to Inamed Silicone Gel Breast Implants Complication Rates

	AUGMENTATION		RECONSTRUCTION		REVISION		LITERATURE
Complication*	**Risk by Pt% (95% CI) MENTOR**	Risk by Pt% (95% CI) INAMED	**Risk by Pt% (95% CI) MENTOR**	Risk by Pt% (95% CI) INAMED	**Risk by Pt% (95% CI) MENTOR**	Risk by Pt% (95% CI) INAMED	Risk by Pt% (95% CI) LITERATURE
Breast mass	**2.4 (1.0, 3.7)**	Not Reported	**3.9 (1.1, 6.6)**	Not Reported	**5.8 (2.5,9.1)**	Not Reported	3
Capsular contracture	**8.2 (5.9,10.6)**	6.7 (4.5, 9.0)	**8.8 (4.9,12.7)**	13.5 (8.8,18.1)	**17.2 (11.9,22.4)**	9.9 (5.8,14.0)	0-73
Granuloma	**0.2 (0,0.5)**	Not Reported	**0 -**	Not Reported	**1.0 (0,2.3)**	Not Reported	Not Reported
Hematoma	**2.6 (1.2,3.9)**	0.8 (0.0, 1.6)	**1.5 (0,3.3)**	0.4 (0.0,1.3)	**3.0 (0.6,5.3)**	0.9 (0.0,2.2)	0-5 7
Hypertrophic scarring	**6.2 (4.2, 8.3)**	1.7 (0.5, 2.8)	**6.4 (3.0,9.8)**	2.4 (0.3,4.5)	**6.0 (2.7,9.3)**	0.5 (0.0,1.5)	4.1
Implant extrusion	**0 -**	0.2 (0.0, 0.6)	**1.2 (0,2.6)**	0.5 (0.0,1.4)	**1.5 (0.0, 3.1)**	0.5 (0.0,1.4)	0-5.4
Implant removal with and without Replacement	**5.1 (3.2,7.1)**	4.7 (2.8, 6.6)	**13.3 (8.8,17.8)**	17.2 (12.1,22.2)	**13.3 (8.4,18.2)**	10.7 (6.4,14.9)	7.5-33
Infection	**1.5 (0.5,2.5)**	0 -	**5.3 (2.5,8.1)**	2.3 (0.3,4.3)	**1.0 (0,2.4)**	1.8 (0.1,3.7)	0-6.3
Inflammation	**0.4 (0,0.9)**	Not Reported	**0 -**	Not Reported	**1.5 (0,3.2)**	Not Reported	Not Reported
Miscarriage	**1.4 (0.4,2.4)**	Not Reported	**0.9 (0, 20)**	Not Reported	**0 -**	Not Reported	Not Reported
New diagnosis of rheumatic disease	**0.6 (0, 1.2)**	Not Reported	**0.4 (0, 1.2)**	Not Reported	**1.0 (0, 2.4)**	Not Reported	Not Reported
Nipple sensation changes	**10.8 (8.1,13.4)**	0.4 (0.0, 1.0)	**3.1 (0,6.3)**	0 -	**8.6 (4.7,12.6)**	0 -	Not Reported
Ptosis	**2.2 (0.9,3.4)**	1.3 (0.3, 2.4)	**6.9 (2, 11.8)**	1.0 (0.0,2.3)	**2.2 (0.06, 4.3)**	0.5 (0.0,1.4)	Not Reported
Recurrent breast cancer	**0 -**	Not Reported	**1.7 (0.05, 3.4)**	Not Reported	**0.5 (0,1.5)**	Not Reported	8-14
Reoperation	**15.0 (11.9,18.0)**	17.1 (13.7, 20.5)	**26.3 (21.7, 31.9)**	36.9 (30.5,43.4)	**26.3 (20.0,32.6)**	29.4 (23.3,35.6)	10-33
Rupture	**0.2 (0,0.7)**	0.9 (0.0, 1.7)	**0.6 (0, 1.8)**	4.8 (1.7,7.9)	**2.5 (0.07,4.9)**	2.7 (0.4,5.0)	0-69
Seroma	**0.9 (0.1,1.7)**	0 6 (0.0, 1.3)	**4.9 (2.2,7.6)**	1.8 (0.1,3.6)	**2.0 (0.06,3.9)**	4.7 (1.9,7.6)	0-2.1

* Excludes mild occurrences of the following: asymmetry, breast pain, calcification, implant malposition/displacement, nipple sensation changes, breast sensation changes, nipple complications, and wrinkling

Table 6.0-B: Comparison of Mentor Core Complication Rates to Mentor Saline-Filled Breast Implants Complication Rates

Complication* CLIFF – SHOULD THESE BE PRESENTED IN ALPHA ORDER?	AUGMENTATION (MENTOR)		RECONSTRUCTION (MENTOR)		LITERATURE
	Risk by Pt% (95% CI) CORE	Risk by Pt% (95% CI) SALINE	**Risk by Pt% (95% CI) CORE**	Risk by Pt% (95% CI) SALINE	Risk by Pt% (95% CI) LITERATURE
Breast mass not associated with implant	**2.4 (1.0, 3.7)**	Not Reported	**3.9 (1.1, 6.6)**	Not Reported	3
Capsular contracture	**8.2 (5.9,10.6)**	9.0 (7.3,10.7)	**8.8 (4.9,12.7)**	30.0 (24.5,34.8)	0-73
Hematoma	**2.6 (1.2,3.9)**	1.5 (0.8,2.2)	**1.5 (0,3.3)**	1.3 (0.2,2.4)	0-5.7
Hypertrophic scarring	**6.2 (4.2, 8.3)**	2.2 (1.3,3.0)	**6.4 (3.0,9.8)**	4.9 (2.6,7.2)	4.1
Implant extrusion	**0 -**	<1	**1.2 (0,2.6)**	2.4 (0.7,4.0)	0-5.4
Implant removal with & without replacement	**4.8 (2.9,6.7)**	8.1 (6.5,9.7)	**13.3 (8.8,17.8)**	26.8 (22.2,31.5)	7.5-33
Infection	**1.5 (0.5,2.5)**	1.7 (1.0,2.5)	**5.3 (2.5,8.1)**	9.0 (6.0,12.1)	0-6.3
Miscarriage	**1.4 (0.4,2.4)**	Not Reported	**0.9 (0, 20)**	Not Reported	Not Reported
Nipple sensation changes	**10.8 (8.1,13.4)**	Not Reported	**3.1 (0,6.3)**	Not Reported	Not Reported
Ptosis	**2.2 (0.9,3.4)**	1.5 (0.8,2.2)	**6.9 (2, 11.8)**	<1	Not Reported
Recurrent breast cancer	**0 -**	Not Reported	**1.7 (0.05, 3.4)**	Not Reported	8-14
Reoperation	**15.0 (11.9,18.0)**	13.2 (11.2,15.2)	**26.3 (21.7, 31.9)**	40.1 (35.0,45.3)	10-33
Rupture/Deflation	**0.2 (0,0.7)**	3.3 (2.2,4.5)	**0.6 (0, 1.8)**	9.2 (5.7,12.7)	0-69
Seroma	**0.9 (0.1,1.7)**	<1	**4.9 (2.2,7.6)**	5.9 (3.6,8.3)	0-2.1

* For CORE data, excludes mild occurrences of the following: asymmetry, breast pain, calcification, implant malposition/displacement, nipple sensation changes, breast sensation changes, nipple complications, and wrinkling.

7.0 REFERENCES

[1] Breast Imaging after Breast Implants. In Radiological Diagnosis of Breast Diseases.
[2]William H. Fitts. Publisher: Western Psychological Services.
[3]Ware, John. (2000). SF 36 Health Survey Update, Spine. 25(24) 3130-3139.
[4]Franzoi, S.L. & Shields, S.A. (1984). The Body-Esteem Scale: Multidimensional structure and sex differences in a college population. Journal of Personality Assessment, 48, 173-178.
[5]Rosenberg, M. (1965). Society and Me Adolescent Self-Image. Princeton, N.J.: Princeton University Press.
[6]Rosenberg M (1986), Conceiving the Self. Malabar, FL: Basic Books.
[7]Morrow GR, Lindke J, Black P. Measurement of Quality of Life in patients: psychometric analyses of the Functional Living Index -- Cancer (FLIC). Qual Life Res 1992; 1:287-96.
[8]Summary of Clinical Data for Mentor Saline-Filled Mammary Prostheses. Nov. 12, 1999.
[9]See www.plasticsurgery.org.
[10]Mentor Corporation. Adjunct Breast Implant Study Study 10th Annual Report. December 2003.
[11]Center for Disease Control, Vital and Health Statistics, Trends in Pregnancies and Pregnancy Rates by Outcome: Estimates for the United States, 1976-96 (Jan. 2000).
[12] Dewey, K.G., L.A. Nommsen-Rivers, M.J. Heinig and R.J. Cohen. 2003. Risk factors for suboptimal infant breastfeeding behavior, delayed onset of lactation, and excess neonatal weight loss. Pediatrics 112 (3 Pt 1):607-619.
[13]American Cancer Society. Breast Cancer Facts & Figures 2003-2004.
[14]Jacobson, D.L., et al. 1997. Epidemiology and estimate population burden of selected autimmune diseases in the United States. Clin. Immunol. Immunopathol. 84(3):223-43.
[15] Wolfe, F., K. Ross, J. Anderson, I.J. Russell and L. Hebert. 1995. The prevalence and characteristics of fibromyalgia in the general population. Arthritis Rheum. 38(1):19-28.
[16]Mancini, G.J., et al. 2002. Parastomal pyoderma gangrenosum: a case report and literature review. Am. Surg. 68(9):824-6.
[17]Campbell, D.T., and Stanley, J.C. 1963. Experimental and Quasi-Experimental Designs for Research. Houghton Mifflin Company, Boston, MA.

Appendix A
Deviations

Post-dated informed consents
407-031-LKG
423-022-SWC

Appendix B
List of Investigators and IRBs

Core Gel Study – Investigators and Approving IRBs

Core Gel Study – Investigators and Approving IRBs

Appendix C
Financial Disclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: February 28, 2006.

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d)

Please mark the applicable checkbox.

☒ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators	
See attached.	

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached

NAME	TITLE
	Director, Clinical Submissions
FIRM/ORGANIZATION	
Mentor	
SIGNATURE	DATE
	27 Aug 04

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

FORM FDA 3454 (2/03)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Form Approved OMB No. 0910-0396
Expiration Date February 28, 2006

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE FILED BY APPLICANT

The following information concerning Investigator Carl Gel who participated as a clinical investigator in the submitted study Name of clinical study Breast Study, is submitted in accordance with 21 CFR part 54. The named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable checkboxes

☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

☐ any significant payments of other sorts made on or after February 2, 1999 from the sponsor of the covered study such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☒ any significant equity interest as defined [illegible], held by the clinical investigator in the sponsor of the covered stu[illegible] ed 5 Jan 04

letter from [illegible]

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to mini[illegible]potential bias of clinical study results by any of the disclosed arrangements or int[illegible]

NAME	TITLE
Mentor	Director, Clinical Sub.
SIGNATURE	DATE
[signature]	27 Aug 04

Paperwork Reduction Act Statement

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Public reporting burden for this collection of information is estimated to average 4 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14-72
Rockville, MD 20857

FORM FDA 3455 (2/03)

PSC Media Arts (301) 443-6740 EF

Cosmetic & Reconstructive
Plastic Surgery

COPY

January 5, 2004

Christine Phillips
Mentor Corporation
201 Mentor Drive
Santa Barbara, CA 93111

Dear Ms. Phillips:

Thank you in advance for your time and consideration. I would greatly appreciate confirmation of your company's receipt of this disclosure in writing at your convenience.

Sincerely,

Attachment to "Certification: Financial Interests and Arrangements of Clinical Investigators"

Site #	Name	Form 3454 Financial Interest	Enrollment			
			Augmentation	Reconstruction	Revision	Total
			26		7	33
			40		3	43
				4	4	8
				8	4	12
				29	8	37
			17			17
				5	1	6
			36	9	13	58
			17	11	9	37
			42		6	48
				5	2	7
				1	3	4
				2		2
			20	10	10	40
					1	4
			52		13	65
				8		8
				4	2	6
			36	1	6	43
				6	2	8
			10	8	6	24
				19	8	27
			1	4	1	6
				1		1
				20	4	24
			32		8	40
			7	4	12	23
				6	1	7
				4		4
			28		7	35
			41	8	9	58
				1	2	3
			2	29	12	43
			22		5	27
			32	1	5	38
			18		6	24
			35	37	12	84
				7	6	13
			33		5	38
					2	2

Appendix D
Data Tables

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis
in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision

Table 1.0

NUMBER OF PATIENTS BY SITE AND INDICATION

Site	Augmentation Patients n (%)	Reconstruction Patients n (%)	Revision Patients n (%)	Overall n (%)
	40 (7.3)	0 (0.0)	9 (4.4)	49 (4.9)
	36 (6.5)	0 (0.0)	10 (4.9)	46 (4.6)
	33 (6.0)	0 (0.0)	5 (2.4)	38 (3.8)
	32 (5.8)	0 (0.0)	6 (2.9)	38 (3.8)
	29 (5.3)	0 (0.0)	7 (3.4)	36 (3.6)
	0 (0.0)	18 (7.2)	8 (3.9)	26 (2.6)
	27 (4.9)	0 (0.0)	7 (3.4)	34 (3.4)
	37 (6.7)	0 (0.0)	7 (3.4)	44 (4.4)
	7 (1.3)	0 (0.0)	6 (2.9)	13 (1.3)
	52 (9.4)	0 (0.0)	12 (5.9)	64 (6.4)
	24 (4.4)	0 (0.0)	5 (2.4)	29 (2.9)
	33 (6.0)	0 (0.0)	8 (3.9)	41 (4.1)
	17 (3.1)	0 (0.0)	0 (0.0)	17 (1.7)
	37 (6.7)	1 (0.4)	6 (2.9)	44 (4.4)
	0 (0.0)	8 (3.2)	6 (2.9)	14 (1.4)

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision

Table 1.0

NUMBER OF PATIENTS BY SITE AND INDICATION

Site	Augmentation Patients n (%)	Reconstruction Patients n (%)	Revision Patients n (%)	Overall n (%)
	19 (3.4)	0 (0.0)	6 (2.9)	25 (2.5)
	42 (7.6)	0 (0.0)	6 (2.9)	48 (4.8)
	1 (0.2)	29 (11.6)	12 (5.9)	42 (4.2)
	0 (0.0)	6 (2.4)	1 (0.5)	7 (0.7)
	0 (0.0)	4 (1.6)	2 (1.0)	6 (0.6)
	17 (3.1)	0 (0.0)	8 (3.9)	25 (2.5)
	41 (7.4)	0 (0.0)	3 (1.5)	44 (4.4)
	1 (0.2)	4 (1.6)	1 (0.5)	6 (0.6)
	10 (1.8)	0 (0.0)	3 (1.5)	13 (1.3)
	0 (0.0)	1 (0.4)	3 (1.5)	4 (0.4)
	0 (0.0)	1 (0.4)	2 (1.0)	3 (0.3)
	0 (0.0)	4 (1.6)	0 (0.0)	4 (0.4)
	0 (0.0)	29 (11.6)	7 (3.4)	36 (3.6)
	0 (0.0)	6 (2.4)	2 (1.0)	8 (0.8)
	0 (0.0)	9 (3.6)	5 (2.4)	14 (1.4)

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis
in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision

Table 1.0

NUMBER OF PATIENTS BY SITE AND INDICATION

Site	Augmentation Patients n (%)	Reconstruction Patients n (%)	Revision Patients n (%)	Overall n (%)
	0 (0.0)	37 (14.7)	4 (2.0)	41 (4.1)
	0 (0.0)	12 (4.8)	3 (1.5)	15 (1.5)
	16 (2.9)	0 (0.0)	7 (3.4)	23 (2.3)
	0 (0.0)	8 (3.2)	0 (0.0)	8 (0.8)
	0 (0.0)	11 (4.4)	2 (1.0)	13 (1.3)
	0 (0.0)	8 (3.2)	3 (1.5)	11 (1.1)
	0 (0.0)	4 (1.6)	5 (2.4)	9 (0.9)
	0 (0.0)	0 (0.0)	2 (1.0)	2 (0.2)
	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.1)
	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.1)
	0 (0.0)	8 (3.2)	0 (0.0)	8 (0.8)
	0 (0.0)	4 (1.6)	2 (1.0)	6 (0.6)
	0 (0.0)	20 (8.0)	3 (1.5)	23 (2.3)
	0 (0.0)	7 (2.8)	4 (2.0)	11 (1.1)
	0 (0.0)	4 (1.6)	4 (2.0)	8 (0.8)

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis
in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision

Table 1.0

NUMBER OF PATIENTS BY SITE AND INDICATION

Site	Augmentation Patients n (%)	Reconstruction Patients n (%)	Revision Patients n (%)	Overall n (%)
	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.2)
	0 (0.0)	4 (1.6)	2 (1.0)	6 (0.6)
	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.1)
	551 (100.0)	251 (100.0)	205 (100.0)	1007 (100.0)

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis
in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision
Patients mixed indications

Table 1.1

INDICATION BY PRIMARY REASON FOR IMPLANTATION

	Augmentation Patients		Reconstruction Patients		Revision Patients		Overall	
Primary Reason for Implantation	Patients n (%)	Implants n (%)	Patients n (%)	Implants n (%)	Patients n (%)	Implants n (%)	Patients n (%)	Implants n (%)
Total Number Implanted	551	1100	251	410	205	386	1007	1896
Augmentation								
Mammary Involution	47 (8.5)	91 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	47 (4.7)	91 (4.8)
Breast Enlargement	488 (88.6)	972 (88.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	488 (48.5)	972 (51.3)
Ptosis	18 (3.3)	34 (3.1)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	19 (1.9)	35 (1.8)
Contralateral Symmetry	1 (0.2)	1 (0.1)	26 (10.4)	26 (6.3)	1 (0.5)	1 (0 3)	28 (2.8)	28 (1.5)
Other	1 (0.2)	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.1)
Reconstruction								
Total-mastectomy-Immediate	0 (0.0)	0 (0.0)	71 (28.3)	93 (22.7)	0 (0.0)	0 (0.0)	71 (7.1)	93 (4.9)
Total-mastectomy-Delayed	0 (0.0)	0 (0.0)	107 (42.6)	151 (36.8)	1 (0.5)	1 (0.3)	108 (10.7)	152 (8.0)
Mixed	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	1 (0.1)	2 (0.1)
Subtotal Mastectomy	0 (0.0)	0 (0.0)	12 (4.8)	16 (3.9)	0 (0.0)	0 (0.0)	12 (1.2)	16 (0.8)
Post-trauma	0 (0.0)	0 (0.0)	3 (1.2)	4 (1.0)	0 (0.0)	0 (0.0)	3 (0.3)	4 (0.2)
Mastopexy	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	1 (0.5)	1 (0.3)	2 (0.2)	2 (0 1)
Congenital Deformity	0 (0.0)	0 (0.0)	60 (23.9)	116 (28.3)	0 (0.0)	0 (0.0)	60 (6.0)	116 (6.1)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

NOTE: Patients and implants may have more than one reason for implantation; therefore, percentages may add to more than 100 percent.

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis
in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision
Patients mixed indications

Table 1.1

INDICATION BY PRIMARY REASON FOR IMPLANTATION

Primary Reason for Implantation	Augmentation Patients		Reconstruction Patients		Revision Patients		Overall	
	Patients n (%)	Implants n (%)	Patients n (%)	Implants n (%)	Patients n (%)	Implants n (%)	Patients n (%)	Implants n (%)
Revision								
Capsular Contracture	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	75 (36.6)	130 (33.7)	75 (7.4)	130 (6.9)
Distortion	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	11 (5.4)	15 (3.9)	11 (1.1)	15 (0.8)
Extrusion	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.3)	1 (0.1)	1 (0.1)
Malposition	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (3.4)	10 (2.6)	7 (0.7)	10 (0.5)
Post-op Hematoma	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Post-op Infection	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ptosis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	11 (5.4)	19 (4.9)	11 (1.1)	19 (1.0)
Rupture	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	40 (19.5)	56 (14.5)	40 (4.0)	56 (3.0)
Size Change-Down	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	10 (4.9)	17 (4.4)	10 (1.0)	17 (0.9)
Size Change-Up	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	32 (15.6)	55 (14.2)	32 (3.2)	55 (2.9)
Valve Retrieval	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	47 (22.9)	78 (20.2)	47 (4.7)	78 (4.1)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)	2 (0.5)	2 (0.2)	2 (0.1)

NOTE: Patients and implants may have more than one reason for implantation; therefore, percentages may add to more than 100 percent.

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision

Table 1.2

REVISION HISTORY
REVISION PATIENTS

Variable	Implants n (%)
Type of Implant being Exchanged	
Gel	178 (46.5)
Saline	197 (51.4)
Missing	8 (2.1)
Total	383 (100.0)
Previous Revisions	
0	256 (66.8)
1	88 (23.0)
2	27 (7.0)
3	6 (1.6)
4	4 (1.0)
5	0 (0.0)
6	1 (0.3)
Missing	1 (0.3)
Total	383 (100.0)
Number of Previous Revisions	
N	382
Mean	0.5
Median	0.0
Standard Deviation	0.83
Minimum	0.0
Maximum	6.0

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis
in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision

Table 1.3

TYPE OF PROCEDURE BY INDICATION

Indication	Procedure: Unilateral — No. of Breast Augmented n(%)	Unilateral — No. of Breast Reconstructed n(%)	Unilateral — No. of Breast Revised n(%)	Unilateral — No. of Patients n(%)	Bilateral — No. of Breast Augmented n(%)	Bilateral — No. of Breast Reconstructed n(%)	Bilateral — No. of Breast Revised n(%)	Bilateral — No. of Patients n(%)
Augmentation								
Mammary Involution	0 (0.0)	0 (0 0)	0 (0.0)	0 (0.0)	91 (8.1)	0 (0.0)	0 (0.0)	47 (5.3)
Breast Enlargement	1 (50.0)	0 (0.0)	0 (0.0)	1 (0.8)	971 (86.3)	0 (0.0)	0 (0.0)	487 (54.8)
Ptosis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	34 (3.0)	1 (0.3)	0 (0.0)	19 (2.1)
Contralateral Symmetry	1 (50.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	27 (9.2)	1 (0.3)	27 (3.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
Reconstruction								
Total-mastectomy	0 (0.0)	87 (94.6)	0 (0.0)	87 (73.7)	0 (0.0)	160 (54.4)	1 (0.3)	93 (10.5)
Immediate	0 (0.0)	41 (44.6)	0 (0.0)	41 (34.7)	0 (0.0)	52 (17.7)	0 (0.0)	30 (3.4)
Delayed	0 (0.0)	46 (50.0)	0 (0.0)	46 (39 0)	0 (0.0)	105 (35.7)	1 (0.3)	62 (7.0)
Mixed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.7)	0 (0.0)	1 (0.1)
Subtotal Mastectomy	0 (0.0)	3 (3.3)	0 (0.0)	3 (2.5)	0 (0.0)	13 (4.4)	0 (0.0)	9 (1.0)
Post-trauma	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.4)	0 (0.0)	3 (0.3)
Mastopexy	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0 0)	1 (0.3)	1 (0.3)	2 (0.2)
Congenital Deformity	0 (0.0)	2 (2.2)	0 (0.0)	2 (1.7)	0 (0.0)	114 (38.8)	0 (0 0)	58 (6.5)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Program Name: Q.\MENTOR\COREGEL\3YEAR\TABLES\T01_3.SAS Creation Date, Time: 16JUL04 10:48

NOTE: Patients and implants may have more than one reason for implantation; therefore, percentages may add to more than 100 percent.

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis
in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision

Table 1.3

TYPE OF PROCEDURE BY INDICATION

Indication	Procedure							
	Unilateral				Bilateral			
	No. of Breast Augmented n(%)	No. of Breast Reconstructed n(%)	No. of Breast Revised n(%)	No. of Patients n(%)	No. of Breast Augmented n(%)	No. of Breast Reconstructed n(%)	No. of Breast Revised n(%)	No. of Patients n(%)
Revision								
Augmentation	0 (0.0)	0 (0.0)	3 (12.5)	3 (2.5)	0 (0.0)	0 (0.0)	286 (79.7)	143 (16.1)
Reconstruction	0 (0.0)	0 (0.0)	21 (87.5)	21 (17.8)	0 (0.0)	0 (0.0)	63 (17.5)	33 (3.7)
Mixed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	10 (2.8)	5 (0.6)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	2 (100.0)	92 (100.0)	24 (100.0)	118 (100.0)	1125 (100.0)	294 (100.0)	359 (100.0)	889 (100.0)

NOTE: Patients and implants may have more than one reason for implantation; therefore, percentages may add to more than 100 percent.

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis
in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision

Table 1.3

TYPE OF PROCEDURE BY INDICATION

	Total			
Indication	No. of Breast Augmented n(%)	No. of Breast Reconstructed n(%)	No. of Breast Revised n(%)	No. of Patients n(%)
Augmentation				
Mammary Involution	91 (8.1)	0 (0.0)	0 (0.0)	47 (4.7)
Breast Enlargement	972 (86.2)	0 (0.0)	0 (0.0)	488 (48.5)
Ptosis	34 (3.0)	0 (0.0)	0 (0.0)	19 (1.9)
Contralateral Symmetry	1 (0.1)	0 (0.0)	0 (0.0)	28 (2.8)
Other	2 (0.2)	0 (0.0)	0 (0.0)	1 (0.1)
Reconstruction				
Total-mastectomy	0 (0.0)	247 (64.0)	0 (0.0)	180 (17.9)
Immediate	0 (0.0)	93 (24.1)	0 (0.0)	71 (7.1)
Delayed	0 (0.0)	151 (39.1)	0 (0.0)	108 (10.7)
Mixed	0 (0.0)	2 (0.5)	0 (0.0)	1 (0.1)
Subtotal Mastectomy	0 (0.0)	16 (4.1)	0 (0.0)	12 (1.2)
Post-trauma	0 (0.0)	4 (1.0)	0 (0.0)	3 (0.3)
Mastopexy	0 (0.0)	1 (0.3)	0 (0.0)	2 (0.2)
Congenital Deformity	0 (0.0)	116 (30.1)	0 (0.0)	60 (6.0)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

NOTE: Patients and implants may have more than one reason for implantation; therefore, percentages may add to more than 100 percent.

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis
in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision

Table 1.3

TYPE OF PROCEDURE BY INDICATION

	Total			
Indication	No. of Breast Augmented n(%)	No. of Breast Reconstructed n(%)	No of Breast Revised n(%)	No. of Patients n(%)
Revision				
Augmentation	0 (0.0)	0 (0.0)	289 (75.5)	146 (14.5)
Reconstruction	0 (0.0)	0 (0.0)	84 (21.9)	54 (5.4)
Mixed	0 (0.0)	0 (0.0)	10 (2.6)	5 (0.5)
Unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	1127 (100.0)	386 (100.0)	383 (100.0)	1007 (100.0)

NOTE: Patients and implants may have more than one reason for implantation; therefore, percentages may add to more than 100 percent.

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis
in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision

Table 1.4

TYPE OF PROCEDURE AND INDICATION BY IMPLANT TYPE

	Procedure							
	Unilateral				Bilateral			
Type of Implant	No. of Breast Augmented n(%)	No. of Breast Reconstructed n(%)	No. of Breast Revised n(%)	No. of Patients n(%)	No. of Breast Augmented n(%)	No. of Breast Reconstructed n(%)	No. of Breast Revised n(%)	No. of Patients n(%)
Smooth-surface Implant	1 (50.0)	39 (42.4)	13 (54.2)	53 (44.9)	782 (69.5)	117 (39.8)	243 (67.7)	571 (64.2)
Texture-surface Implant	1 (50.0)	53 (57.6)	11 (45.8)	65 (55.1)	343 (30.5)	177 (60.2)	116 (32.3)	318 (35.8)
Total	2 (100.0)	92 (100.0)	24 (100.0)	118 (100.0)	1125 (100.0)	294 (100.0)	359 (100.0)	889 (100.0)

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis
in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision

Table 1.4

TYPE OF PROCEDURE AND INDICATION BY IMPLANT TYPE

	Total			
Type of Implant	No. of Breast Augmented n(%)	No. of Breast Reconstructed n(%)	No. of Breast Revised n(%)	No. of Patients n(%)
Smooth-surface Implant	783 (69.5)	156 (40.4)	256 (66.8)	624 (62.0)
Texture-surface Implant	344 (30.5)	230 (59.6)	127 (33.2)	383 (38.0)
Total	1127 (100.0)	386 (100.0)	383 (100.0)	1007 (100.0)

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis
in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision

Table 1.5

INDICATION BY IMPLANT TYPE

	Augmentation Patients		Reconstruction Patients			Revision Patients			
Type of Implant	No. of Breast Augmented n(%)	No. of Patients n(%)	No. of Breast Augmented n(%)	No. of Breast Reconstructed n(%)	No. of Patients n(%)	No. of Breast Augmented n(%)	No. of Breast Reconstructed n(%)	No. of Breast Revised n(%)	No. of Patients n(%)
Smooth-surface Implant	767 (69.7)	384 (69.7)	16 (61.5)	155 (40.4)	105 (41.8)	0 (0.0)	1 (50.0)	256 (66.8)	135 (65.9)
Texture-surface Implant	333 (30.3)	167 (30.3)	10 (38.5)	229 (59.6)	146 (58.2)	1 (100.0)	1 (50.0)	127 (33.2)	70 (34.1)
Total	1100 (100.0)	551 (100.0)	26 (100.0)	384 (100.0)	251 (100.0)	1 (100.0)	2 (100.0)	383 (100.0)	205 (100.0)

Core Gel Study of the Safety and Effectiveness of the Mentor Round Gel-Filled Mammary Prosthesis
in Patients Who Are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction or Revision

Table 1.5

INDICATION BY IMPLANT TYPE

	Overall			
Type of Implant	No. of Breast Augmented n(%)	No. of Breast Reconstructed n(%)	No. of Breast Revised n(%)	No. of Patients n(%)
Smooth-surface Implant	783 (69.5)	156 (40.4)	256 (66.8)	624 (62.0)
Texture-surface Implant	344 (30.5)	230 (59.6)	127 (33.2)	383 (38.0)
Total	1127 (100.0)	386 (100.0)	383 (100.0)	1007 (100.0)